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\* \* \* \* \* \* \* \* \* \* \* \* \* Welcome to STN International \* \* \* \* \* \* \* \* \* \* \*

NEWS	1		Web Page for STN Seminar Schedule - N. America
NEWS	2	AUG 06	CAS REGISTRY enhanced with new experimental property tags
NEWS	3	AUG 06	FSTA enhanced with new thesaurus edition
NEWS	4	AUG 13	CA/CAplus enhanced with additional kind codes for granted patents
NEWS	5	AUG 20	CA/CAplus enhanced with CAS indexing in pre-1907 records
NEWS	6	AUG 27	Full-text patent databases enhanced with predefined patent family display formats from INPADOCDB
NEWS	7	AUG 27	USPATOLD now available on STN
NEWS	8	AUG 28	CAS REGISTRY enhanced with additional experimental spectral property data
NEWS	9	SEP 07	STN AnaVist, Version 2.0, now available with Derwent World Patents Index
NEWS	10	SEP 13	FORIS renamed to SOFIS
NEWS	11	SEP 13	INPADOCDB enhanced with monthly SDI frequency
NEWS	12	SEP 17	CA/CAplus enhanced with printed CA page images from 1967-1998
NEWS	13	SEP 17	CAplus coverage extended to include traditional medicine patents
NEWS	14	SEP 24	EMBASE, EMBAL, and LEMBASE reloaded with enhancements
NEWS	15	OCT 02	CA/CAplus enhanced with pre-1907 records from Chemisches Zentralblatt
NEWS	16	OCT 19	BEILSTEIN updated with new compounds
NEWS	17	NOV 15	Derwent Indian patent publication number format enhanced
NEWS	18	NOV 19	WPIX enhanced with XML display format
NEWS	19	NOV 30	ICSD reloaded with enhancements
NEWS	20	DEC 04	LINPADOCDB now available on STN
NEWS	21	DEC 14	BEILSTEIN pricing structure to change
NEWS	22	DEC 17	USPATOLD added to additional database clusters
NEWS	23	DEC 17	IMSDRUGCONF removed from database clusters and STN
NEWS	24	DEC 17	DGENE now includes more than 10 million sequences
NEWS	25	DEC 17	TOXCENTER enhanced with 2008 MeSH vocabulary in MEDLINE segment
NEWS	26	DEC 17	MEDLINE and LMEDLINE updated with 2008 MeSH vocabulary
NEWS	27	DEC 17	CA/CAplus enhanced with new custom IPC display formats
NEWS	28	DEC 17	STN Viewer enhanced with full-text patent content from USPATOLD
NEWS	29	JAN 02	STN pricing information for 2008 now available
NEWS	30	JAN 16	CAS patent coverage enhanced to include exemplified prophetic substances
NEWS	31	JAN 28	USPATFULL, USPAT2, and USPATOLD enhanced with new custom IPC display formats
NEWS	32	JAN 28	MARPAT searching enhanced

NEWS 33 JAN 28 USGENE now provides USPTO sequence data within 3 days of publication  
NEWS 34 JAN 28 TOXCENTER enhanced with reloaded MEDLINE segment  
NEWS 35 JAN 28 MEDLINE and LMEDLINE reloaded with enhancements  
NEWS 36 FEB 08 STN Express, Version 8.3, now available  
NEWS 37 FEB 20 PCI now available as a replacement to DPCI

NEWS EXPRESS FEBRUARY 08 CURRENT WINDOWS VERSION IS V8.3,  
AND CURRENT DISCOVER FILE IS DATED 20 FEBRUARY 2008

NEWS HOURS STN Operating Hours Plus Help Desk Availability  
NEWS LOGIN Welcome Banner and News Items  
NEWS IPC8 For general information regarding STN implementation of IPC 8

Enter NEWS followed by the item number or name to see news on that specific topic.

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\* \*

FILE 'HOME' ENTERED AT 20:25:33 ON 22 FEB 2008

=> file reg	SINCE FILE	TOTAL
COST IN U.S. DOLLARS	ENTRY	SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 20:25:48 ON 22 FEB 2008  
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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 21 FEB 2008 HIGHEST RN 1005032-28-9  
DICTIONARY FILE UPDATES: 21 FEB 2008 HIGHEST RN 1005032-28-9

New CAS Information Use Policies, enter HELP USAGETERMS for details.

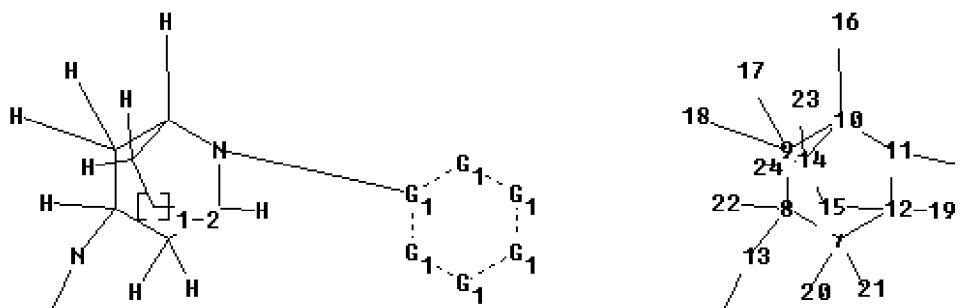
TSCA INFORMATION NOW CURRENT THROUGH January 9, 2008.

Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

<http://www.cas.org/support/stngen/stndoc/properties.html>

=>  
Uploading C:\Program Files\Stnexp\Queries\10518114allow.str



chain nodes :

13 16 17 18 19 20 21 22 23 24 31

ring nodes :

1 2 3 4 5 6 7 8 9 10 11 12 14 15

chain bonds :

3-11 7-20 7-21 8-13 8-22 9-17 9-18 10-16 12-19 13-31 14-23 14-24

ring bonds :

1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-12 8-9 9-10 10-11 10-14 11-12 12-15 14-15

exact/norm bonds :

1-2 1-6 2-3 3-4 3-11 4-5 5-6 7-8 7-12 7-20 7-21 8-9 8-13 8-22 9-10

9-17 9-18 10-11 10-14 10-16 11-12 12-15 12-19 13-31 14-15 14-23 14-24

isolated ring systems :

containing 1 : 7 :

G1:C,N

G2:C,H

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom

11:Atom 12:Atom 13:CLASS 14:Atom 15:Atom 16:CLASS 17:CLASS 18:CLASS

19:CLASS 20:CLASS 21:CLASS

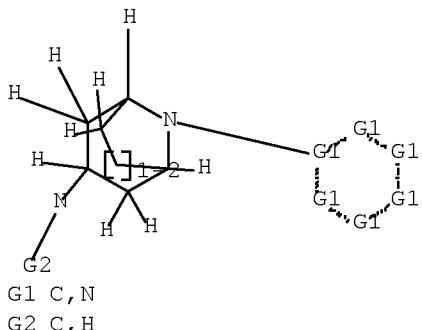
22:CLASS 23:CLASS 24:CLASS 31:CLASS

L1 STRUCTURE UPLOADED

=> d l1

L1 HAS NO ANSWERS

L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> s l1 full

FULL SEARCH INITIATED 20:26:47 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 110328 TO ITERATE

100.0% PROCESSED 110328 ITERATIONS  
SEARCH TIME: 00.00.01

214 ANSWERS

L2 214 SEA SSS FUL L1

=> file caplus

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

FULL ESTIMATED COST

ENTRY

SESSION

178.82

179.03

FILE 'CAPLUS' ENTERED AT 20:26:52 ON 22 FEB 2008

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FILE COVERS 1907 - 22 Feb 2008 VOL 148 ISS 9

FILE LAST UPDATED: 21 Feb 2008 (20080221/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply.  
They are available for your review at:

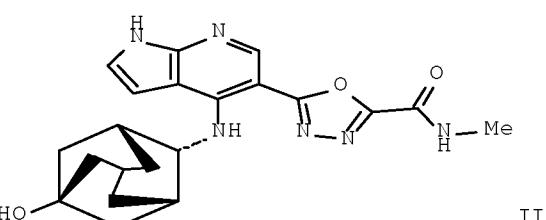
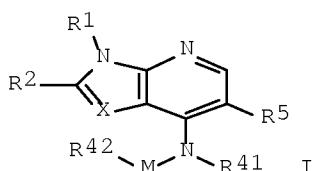
<http://www.cas.org/infopolicy.html>

=> s 12 full  
L3            19 L2

=> d ibib abs hitstr tot

L3 ANSWER 1 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN  
ACCESSION NUMBER: 2007:757385 CAPLUS Full-text  
DOCUMENT NUMBER: 147:166304  
TITLE: Preparation of heterocyclic compounds as janus kinase 3 inhibitors  
INVENTOR(S): Inoue, Takayuki; Tanaka, Akira; Nakai, Kazuo; Sasaki, Hiroshi; Takahashi, Fumie; Shirakami, Shohei; Hatanaka, Keiko; Nakajima, Yutaka; Mukoyoshi, Koichiro; Hamaguchi, Hisao; Kunikawa, Shigeki; Higashi, Yasuyuki  
PATENT ASSIGNEE(S): Astellas Pharma Inc., Japan  
SOURCE: PCT Int. Appl., 266pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 2  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007077949	A1	20070712	WO 2006-JP326327	20061225
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
PRIORITY APPLN. INFO.:			JP 2005-378858	A 20051228
OTHER SOURCE(S):		MARPAT 147:166304		
GI				



AB The title heterocyclic compds. I [wherein X = N or (un)substituted CH; M = a bond or CH<sub>2</sub>; R<sub>1</sub> and R<sub>2</sub> = independently H or (un)substituted alkyl; R<sub>41</sub> = H or (un)substituted heteroaryl; R<sub>42</sub> = an (un)substituted bridged ring group; R<sub>5</sub> = halo, CN, acyl, etc.; or R<sub>41</sub> and R<sub>5</sub> form a ring.] or pharmaceutically acceptable salts thereof were prepared as janus kinase 3 (JAK3) inhibitors. For example, II was prepared in a multi-step synthesis. The compds. are useful for treating or preventing various immune diseases, such as rejection during organ/tissue transplantation, autoimmune diseases, multiple sclerosis, rheumatoid arthritis, psoriasis, asthma, etc.

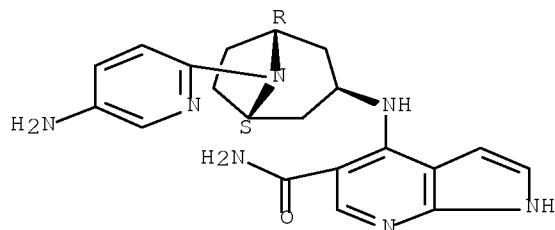
IT 944117-13-9P 944122-15-0P 944122-18-3P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
(drug candidate; preparation of heterocyclic compds. as JAK3 inhibitors)

RN 944117-13-9 CAPLUS

CN 1H-Pyrrolo[2,3-b]pyridine-5-carboxamide, 4-[(3-exo)-8-(5-amino-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]- (CA INDEX NAME)

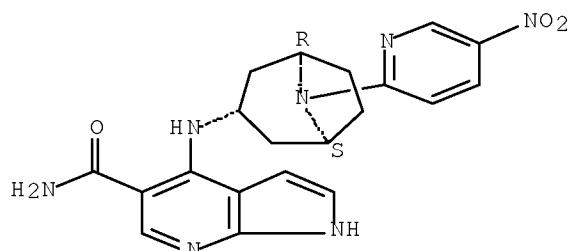
Relative stereochemistry.



RN 944122-15-0 CAPLUS

CN 1H-Pyrrolo[2,3-b]pyridine-5-carboxamide, 4-[(3-exo)-8-(5-nitro-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]- (CA INDEX NAME)

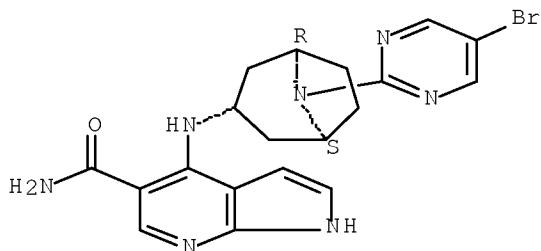
Relative stereochemistry.



RN 944122-18-3 CAPLUS

CN 1H-Pyrrolo[2,3-b]pyridine-5-carboxamide, 4-[(3-exo)-8-(5-bromo-2-pyrimidinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]- (CA INDEX NAME)

Relative stereochemistry.



IT 944117-21-9P 944117-22-0P 944117-26-4P  
944117-44-6P 944117-52-6P 944118-18-7P  
944118-20-1P 944118-46-1P 944121-64-6P  
944121-87-3P 944121-88-4P 944121-89-5P  
944121-90-8P 944121-91-9P 944121-93-1P  
944121-94-2P 944121-98-6P 944122-13-8P  
944122-14-9P 944122-16-1P 944122-17-2P  
944122-19-4P 944122-21-8P 944122-23-0P  
944122-25-2P 944122-26-3P 944122-28-5P  
944122-29-6P 944122-31-0P 944122-32-1P  
944135-23-3P 944135-24-4P 944135-25-5P

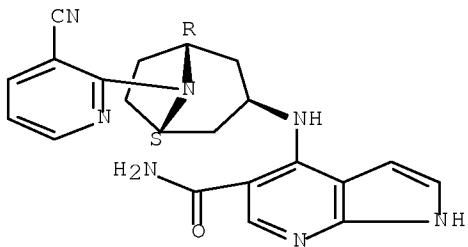
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug candidate; preparation of heterocyclic compds. as JAK3 inhibitors)

RN 944117-21-9 CAPLUS

CN 1H-Pyrrolo[2,3-b]pyridine-5-carboxamide, 4-[(3-exo)-8-(3-cyano-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]- (CA INDEX NAME)

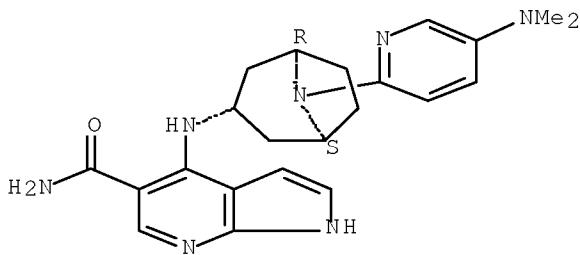
Relative stereochemistry.



RN 944117-22-0 CAPLUS

CN 1H-Pyrrolo[2,3-b]pyridine-5-carboxamide, 4-[(3-exo)-8-[5-(dimethylamino)-2-pyridinyl]-8-azabicyclo[3.2.1]oct-3-yl]amino]- (CA INDEX NAME)

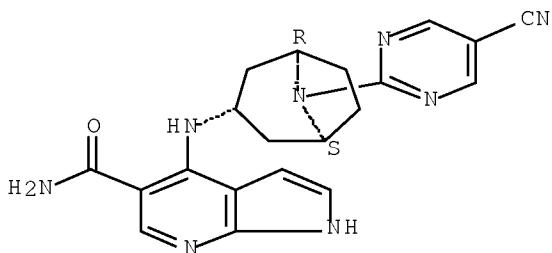
Relative stereochemistry.



RN 944117-26-4 CAPLUS

CN 1H-Pyrrolo[2,3-b]pyridine-5-carboxamide, 4-[(3-exo)-8-(5-cyano-2-pyrimidinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]- (CA INDEX NAME)

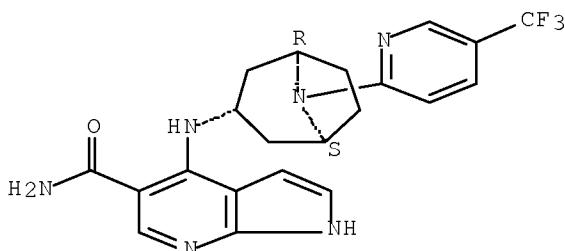
Relative stereochemistry.



RN 944117-44-6 CAPLUS

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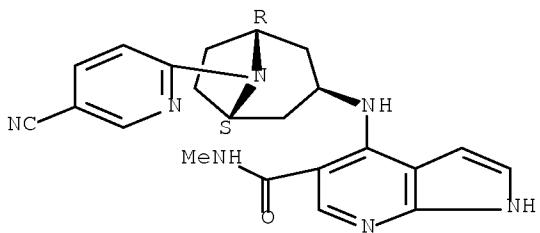
Relative stereochemistry.



RN 944117-52-6 CAPLUS

CN 1H-Pyrrolo[2,3-b]pyridine-5-carboxamide, 4-[(3-exo)-8-(5-cyano-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]-N-methyl- (CA INDEX NAME)

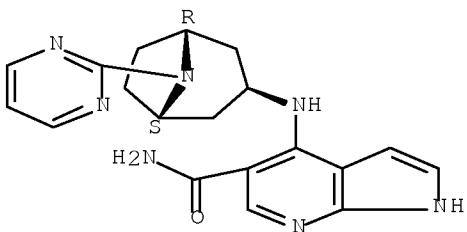
Relative stereochemistry.



RN 944118-18-7 CAPLUS

CN 1H-Pyrrolo[2,3-b]pyridine-5-carboxamide, 4-[[[(3-exo)-8-(2-pyrimidinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]- (CA INDEX NAME)

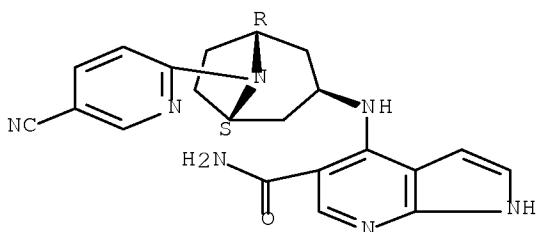
Relative stereochemistry.



RN 944118-20-1 CAPLUS

CN 1H-Pyrrolo[2,3-b]pyridine-5-carboxamide, 4-[[[(3-exo)-8-(5-cyano-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]- (CA INDEX NAME)

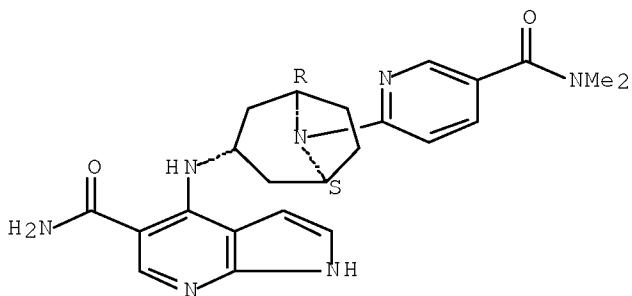
Relative stereochemistry.



RN 944118-46-1 CAPLUS

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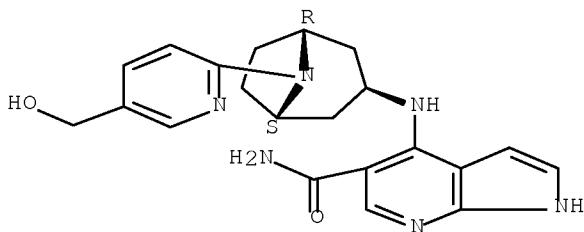
Relative stereochemistry.



RN 944121-64-6 CAPLUS

CN 1H-Pyrrolo[2,3-b]pyridine-5-carboxamide, 4-[(3-exo)-8-[5-(hydroxymethyl)-2-pyridinyl]-8-azabicyclo[3.2.1]oct-3-yl]amino]- (CA INDEX NAME)

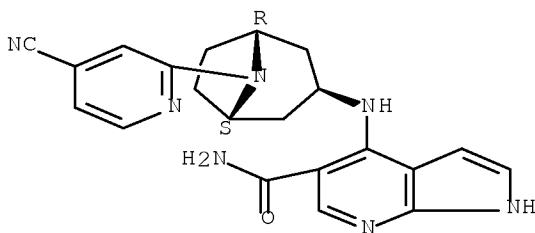
Relative stereochemistry.



RN 944121-87-3 CAPLUS

CN 1H-Pyrrolo[2,3-b]pyridine-5-carboxamide, 4-[(3-exo)-8-(4-cyano-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]- (CA INDEX NAME)

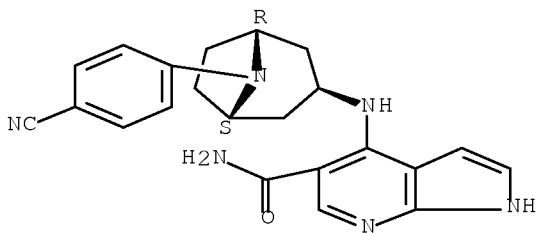
Relative stereochemistry.



RN 944121-88-4 CAPLUS

CN 1H-Pyrrolo[2,3-b]pyridine-5-carboxamide, 4-[(3-exo)-8-(4-cyanophenyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]- (CA INDEX NAME)

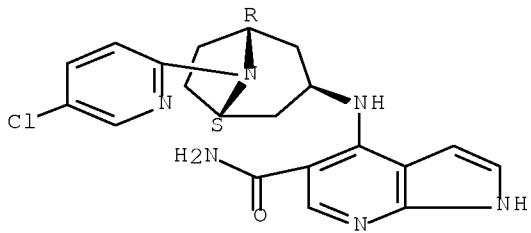
Relative stereochemistry.



RN 944121-89-5 CAPLUS

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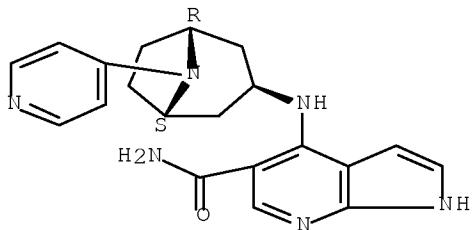
Relative stereochemistry.



RN 944121-90-8 CAPLUS

CN 1H-Pyrrolo[2,3-b]pyridine-5-carboxamide, 4-[[ (3-exo)-8-(4-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]- (CA INDEX NAME)

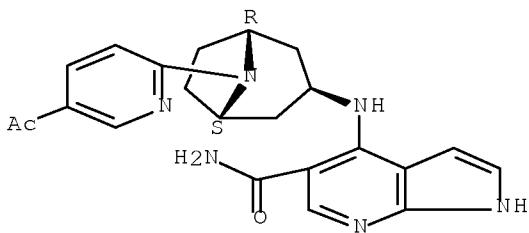
Relative stereochemistry.



RN 944121-91-9 CAPLUS

CN 1H-Pyrrolo[2,3-b]pyridine-5-carboxamide, 4-[[ (3-exo)-8-(5-acetyl-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]- (CA INDEX NAME)

Relative stereochemistry.



RN 944121-93-1 CAPLUS

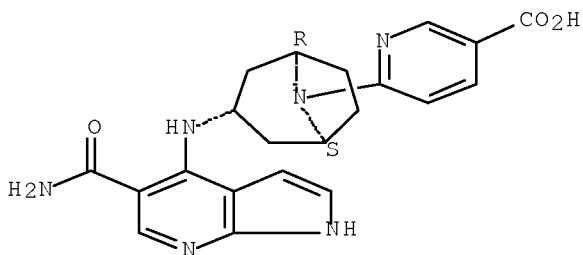
CN 3-Pyridinecarboxylic acid, 6-[(3-exo)-3-[[5-(aminocarbonyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]amino]-8-azabicyclo[3.2.1]oct-8-yl]-, 2,2,2-trifluoroacetate (1:3) (CA INDEX NAME)

CM 1

CRN 944121-92-0

CMF C21 H22 N6 O3

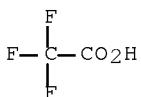
Relative stereochemistry.



CM 2

CRN 76-05-1

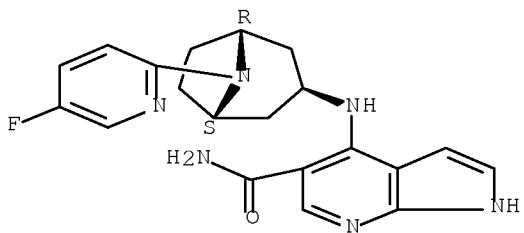
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RN 944121-94-2 CAPLUS

CN 1H-Pyrrolo[2,3-b]pyridine-5-carboxamide, 4-[(3-exo)-8-(5-fluoro-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]- (CA INDEX NAME)

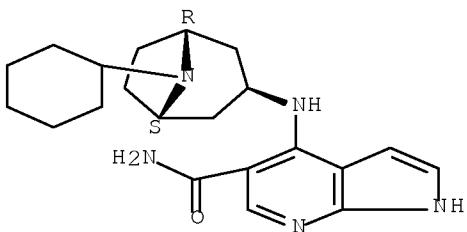
Relative stereochemistry.



RN 944121-98-6 CAPLUS

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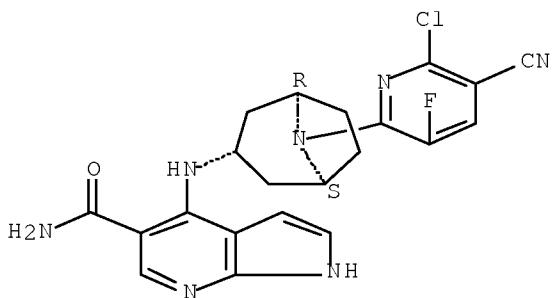
Relative stereochemistry.



RN 944122-13-8 CAPLUS

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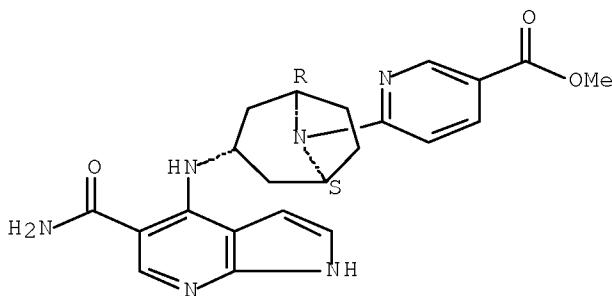
Relative stereochemistry.



RN 944122-14-9 CAPLUS

CN 3-Pyridinecarboxylic acid, 6-[(3-exo)-3-[[5-(aminocarbonyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]amino]-8-azabicyclo[3.2.1]oct-8-yl]-, methyl ester (CA INDEX NAME)

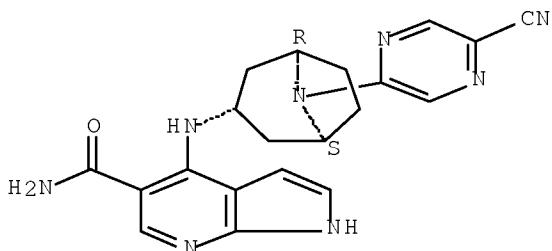
Relative stereochemistry.



RN 944122-16-1 CAPLUS

CN 1H-Pyrrolo[2,3-b]pyridine-5-carboxamide, 4-[(3-exo)-8-(5-cyano-2-pyrazinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]- (CA INDEX NAME)

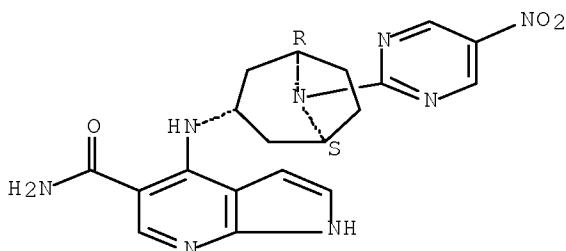
Relative stereochemistry.



RN 944122-17-2 CAPLUS

CN 1H-Pyrrolo[2,3-b]pyridine-5-carboxamide, 4-[(3-exo)-8-(5-nitro-2-pyrimidinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]- (CA INDEX NAME)

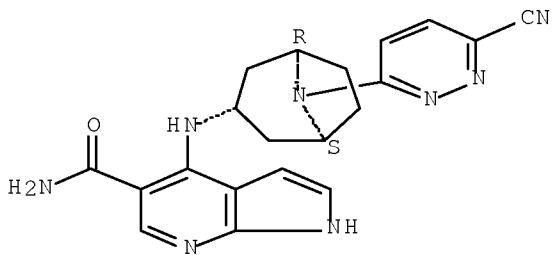
Relative stereochemistry.



RN 944122-19-4 CAPLUS

CN 1H-Pyrrolo[2,3-b]pyridine-5-carboxamide, 4-[(3-exo)-8-(6-cyano-3-pyridazinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]- (CA INDEX NAME)

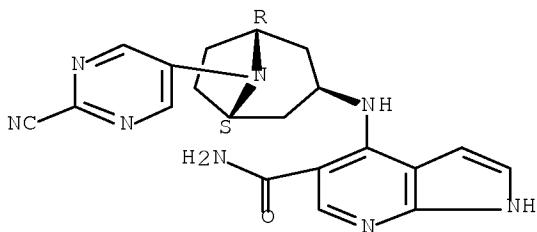
Relative stereochemistry.



RN 944122-21-8 CAPLUS

CN 1H-Pyrrolo[2,3-b]pyridine-5-carboxamide, 4-[(3-exo)-8-(2-cyano-5-pyrimidinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]- (CA INDEX NAME)

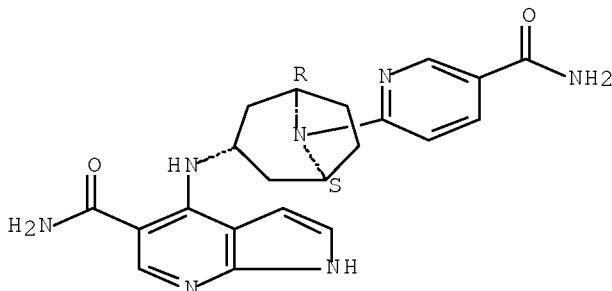
Relative stereochemistry.



RN 944122-23-0 CAPLUS

CN 1H-Pyrrolo[2,3-b]pyridine-5-carboxamide, 4-[(3-exo)-8-[5-(aminocarbonyl)-2-pyridinyl]-8-azabicyclo[3.2.1]oct-3-yl]amino]- (CA INDEX NAME)

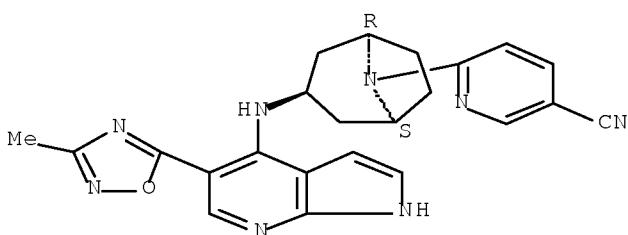
Relative stereochemistry.



RN 944122-25-2 CAPLUS

CN 3-Pyridinecarbonitrile, 6-[(3-endo)-3-[(5-(3-methyl-1,2,4-oxadiazol-5-yl)-1H-pyrrolo[2,3-b]pyridin-4-yl)amino]-8-azabicyclo[3.2.1]oct-8-yl]- (CA INDEX NAME)

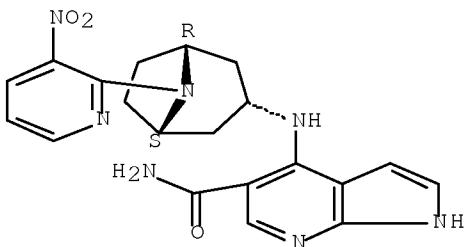
Relative stereochemistry.



RN 944122-26-3 CAPLUS

CN 1H-Pyrrolo[2,3-b]pyridine-5-carboxamide, 4-[[3-endo)-8-(3-nitro-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]- (CA INDEX NAME)

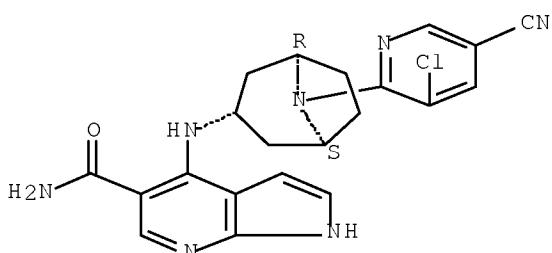
Relative stereochemistry.



RN 944122-28-5 CAPLUS

CN 1H-Pyrrolo[2,3-b]pyridine-5-carboxamide, 4-[[3-exo)-8-(3-chloro-5-cyano-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]- (CA INDEX NAME)

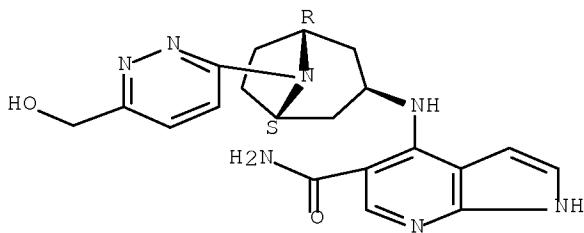
Relative stereochemistry.



RN 944122-29-6 CAPLUS

CN 1H-Pyrrolo[2,3-b]pyridine-5-carboxamide, 4-[[3-exo)-8-[6-(hydroxymethyl)-3-pyridazinyl]-8-azabicyclo[3.2.1]oct-3-yl]amino]- (CA INDEX NAME)

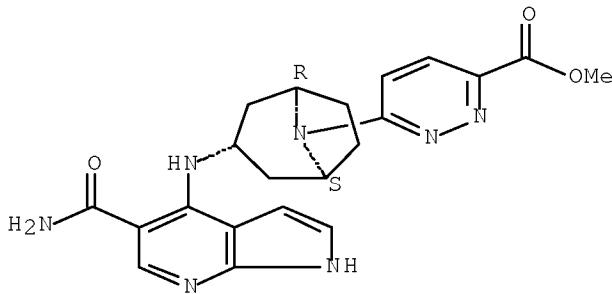
Relative stereochemistry.



RN 944122-31-0 CAPLUS

CN 3-Pyridazinecarboxylic acid, 6-[(3-exo)-3-[[5-(aminocarbonyl)-1H-pyrrolo[2,3-b]pyridin-4-yl]amino]-8-azabicyclo[3.2.1]oct-8-yl]-, methyl ester (CA INDEX NAME)

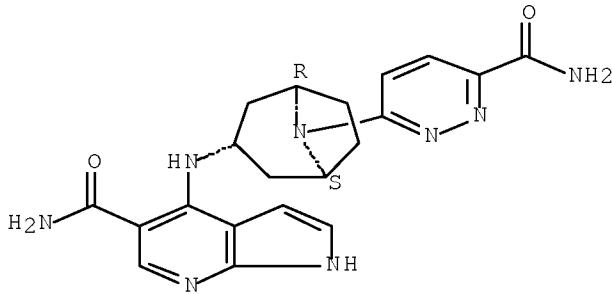
Relative stereochemistry.



RN 944122-32-1 CAPLUS

CN 1H-Pyrrolo[2,3-b]pyridine-5-carboxamide, 4-[(3-exo)-8-[6-(aminocarbonyl)-3-pyridazinyl]-8-azabicyclo[3.2.1]oct-3-yl]amino]- (CA INDEX NAME)

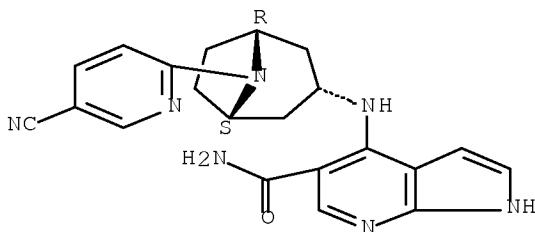
Relative stereochemistry.



RN 944135-23-3 CAPLUS

CN 1H-Pyrrolo[2,3-b]pyridine-5-carboxamide, 4-[(3-endo)-8-(5-cyano-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]- (CA INDEX NAME)

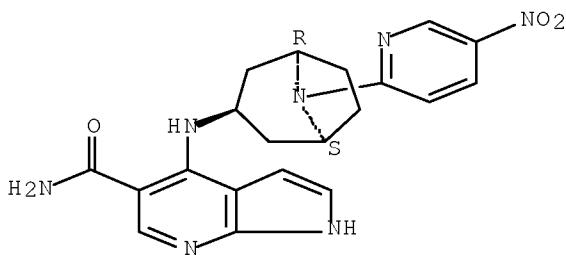
Relative stereochemistry.



RN 944135-24-4 CAPLUS

CN 1H-Pyrrolo[2,3-b]pyridine-5-carboxamide, 4-[[ (3-endo)-8-(5-nitro-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]- (CA INDEX NAME)

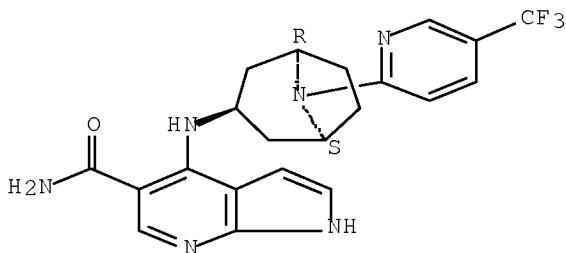
Relative stereochemistry.



RN 944135-25-5 CAPLUS

CN 1H-Pyrrolo[2,3-b]pyridine-5-carboxamide, 4-[[ (3-endo)-8-[5-(trifluoromethyl)-2-pyridinyl]-8-azabicyclo[3.2.1]oct-3-yl]amino]- (CA INDEX NAME)

Relative stereochemistry.



IT 944122-57-0P 944123-89-1P

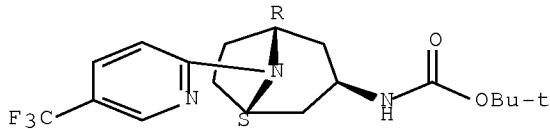
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(intermediate; preparation of heterocyclic compds. as JAK3 inhibitors)

RN 944122-57-0 CAPLUS

CN Carbamic acid, N-[(3-exo)-8-[5-(trifluoromethyl)-2-pyridinyl]-8-

azabicyclo[3.2.1]oct-3-yl-, 1,1-dimethylethyl ester (CA INDEX NAME)

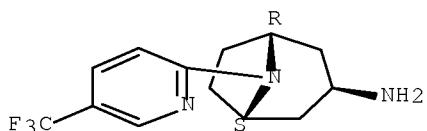
Relative stereochemistry.



RN 944123-89-1 CAPLUS

CN 8-Azabicyclo[3.2.1]octan-3-amine, 8-[5-(trifluoromethyl)-2-pyridinyl]-, (3-exo)- (CA INDEX NAME)

Relative stereochemistry.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2007:409606 CAPLUS [Full-text](#)

DOCUMENT NUMBER: 146:401834

TITLE: Preparation of azabicyclo[2.2.1]octane derivatives as pesticides

INVENTOR(S): Hamamoto, Isami; Takahashi, Jun; Yano, Makio; Kawaguchi, Masahiro; Hanai, Daisuke; Iwasa, Takao

PATENT ASSIGNEE(S): Nippon Soda Co., Ltd., Japan

SOURCE: PCT Int. Appl., 97pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007040280	A1	20070412	WO 2006-JP320126	20061006
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,				

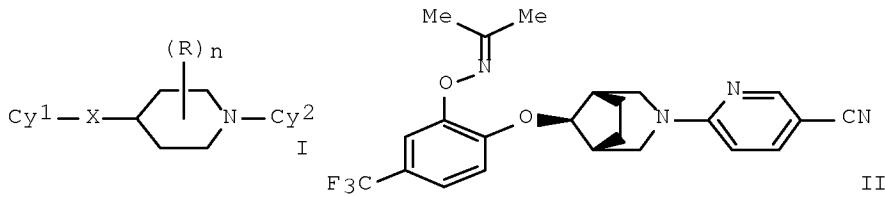
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,  
KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.:

JP 2005-294126	A 20051006
JP 2005-294127	A 20051006
JP 2005-297803	A 20051012
JP 2005-297804	A 20051012
JP 2006-16877	A 20060125
JP 2006-182314	A 20060630

OTHER SOURCE(S): MARPAT 146:401834

GI



AB The title compds. I [wherein Cy1 = (un)substituted heterocyclyl; Cy2 = (un)substituted cyclyl, heterocyclyl, etc.; n = 0-9; X = O, S, SO, SO<sub>2</sub>, or (un)substituted NH; R = OH, halo, (un)substituted NH<sub>2</sub>, etc.; or two R's form a ring] are prepared as pest control agents. For example, the compound II was prepared in a multi-step synthesis. Some of compds. I showed excellent pesticidal activities in tests.

IT 933797-20-7P 933797-68-3P 933797-69-4P  
933797-70-7P 933797-71-8P

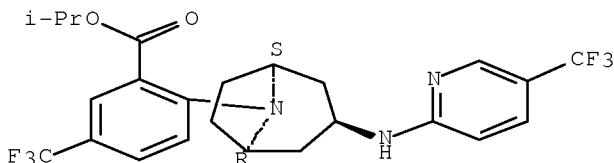
RL: AGR (Agricultural use); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)

(pesticide; preparation of azabicyclo[2.2.1]octane derivs. as pesticides)

RN 933797-20-7 CAPLUS

CN Benzoic acid, 5-(trifluoromethyl)-2-[(3-endo)-3-[5-(trifluoromethyl)-2-pyridinyl]amino]-8-azabicyclo[3.2.1]oct-8-yl-, 1-methylethyl ester (CA INDEX NAME)

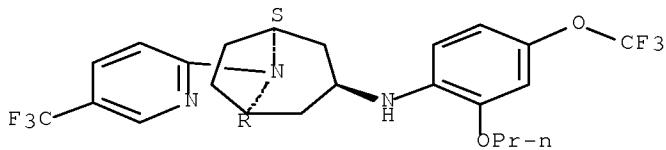
Relative stereochemistry.



RN 933797-68-3 CAPLUS

CN 8-Azabicyclo[3.2.1]octan-3-amine, N-[2-propoxy-4-(trifluoromethoxy)phenyl]-8-[5-(trifluoromethyl)-2-pyridinyl]-, (3-endo)- (CA INDEX NAME)

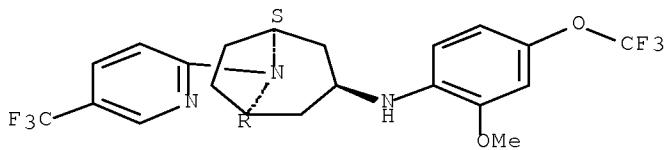
Relative stereochemistry.



RN 933797-69-4 CAPLUS

CN 8-Azabicyclo[3.2.1]octan-3-amine, N-[2-methoxy-4-(trifluoromethoxy)phenyl]-8-[5-(trifluoromethyl)-2-pyridinyl]-, (3-endo)- (CA INDEX NAME)

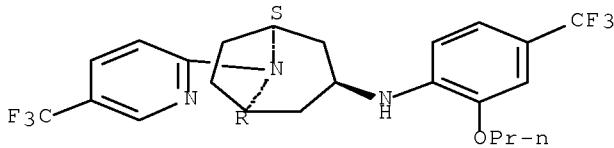
Relative stereochemistry.



RN 933797-70-7 CAPLUS

CN 8-Azabicyclo[3.2.1]octan-3-amine, N-[2-propoxy-4-(trifluoromethyl)phenyl]-8-[5-(trifluoromethyl)-2-pyridinyl]-, (3-exo)- (CA INDEX NAME)

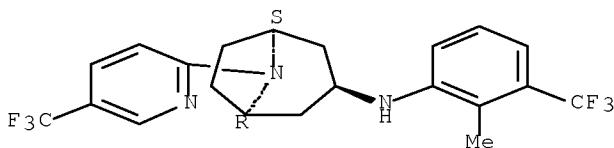
Relative stereochemistry.



RN 933797-71-8 CAPLUS

CN 8-Azabicyclo[3.2.1]octan-3-amine, N-[2-methoxy-4-(trifluoromethoxy)phenyl]-8-[5-(trifluoromethyl)-2-pyridinyl]-, (3-endo)- (CA INDEX NAME)

Relative stereochemistry.



REFERENCE COUNT:

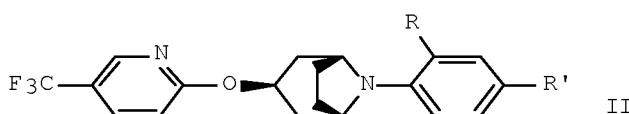
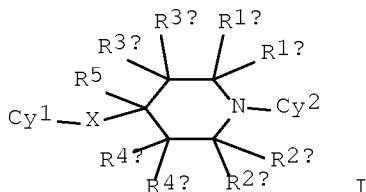
7

THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 3 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 2007:405401 CAPLUS Full-text  
 DOCUMENT NUMBER: 146:421857  
 TITLE: Preparation of bridged cyclic amine compounds as pest control agents  
 INVENTOR(S): Hamamoto, Isami; Takahashi, Jun; Yano, Makio;  
 Kawaguchi, Masahiro; Hanai, Daisuke; Iwasa, Takao  
 PATENT ASSIGNEE(S): Nippon Soda Co., Ltd., Japan  
 SOURCE: PCT Int. Appl., 98pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007040282	A1	20070412	WO 2006-JP320133	20061006
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GO, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
PRIORITY APPLN. INFO.:			JP 2005-294126	A 20051006
			JP 2005-294127	A 20051006
			JP 2005-297803	A 20051012
			JP 2005-297804	A 20051012
			JP 2006-16877	A 20060125
			JP 2006-182314	A 20060630

OTHER SOURCE(S): MARPAT 146:421857  
 GI



AB Title compds. I [Cy1 = (un)substituted aromatic ring; X = oxygen, sulfur, (un)substituted nitrogen, etc.; R1a and R2a, R1a and R4a, R2a and R3a, or R3a and R4a may combine to form a saturated ring.; R1a-R4a, R1b-R4b and R5 = H, hydroxy, halo, etc.; Cy2 = (un)substituted aromatic ring; when R1a and R2a may combine to form saturated ring and Cy1 is a (un)substituted Ph, Cy2 is a (un)substituted aromatic heterocycle.; when Cy1 is a (un)substituted Ph and Cy2 is a pyridin-2-yl, Cy2 is a pyridin-2-yl substituted with one or more cyano groups.], salts or N-oxides thereof were prepared. For example, reaction of tropine with 2-chloro-5-trifluoromethylpyridine followed by treatment with 2,2,2-trichloroethyl chloroformate, reduction using Zn/acetic acid and O-arylation with 2-fluoro-5-trifluoromethylbenzaldehyde afforded compound II [R = CHO; R' = CF<sub>3</sub>]. Compound II [R = OCH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>; R' = CF<sub>3</sub>] controlled two-spotted spider mite by 100%.

IT 933797-20-7P 933797-68-3P 933797-69-4P  
933797-70-7P 933797-71-8P

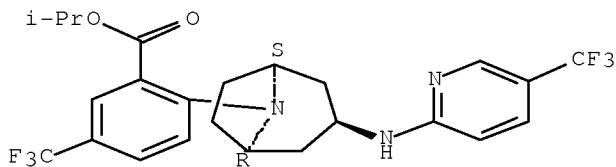
RL: AGR (Agricultural use); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of bridged cyclic amine compds. as pest control agents)

RN 933797-20-7 CAPLUS

CN Benzoic acid, 5-(trifluoromethyl)-2-[(3-endo)-3-[[5-(trifluoromethyl)-2-pyridinyl]amino]-8-azabicyclo[3.2.1]oct-8-yl]-, 1-methylethyl ester (CA INDEX NAME)

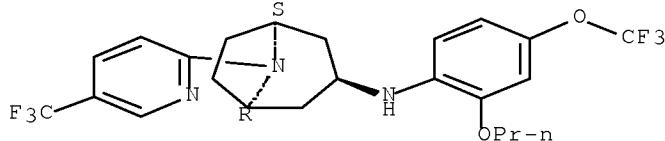
Relative stereochemistry.



RN 933797-68-3 CAPLUS

CN 8-Azabicyclo[3.2.1]octan-3-amine, N-[2-propoxy-4-(trifluoromethoxy)phenyl]-8-[5-(trifluoromethyl)-2-pyridinyl]-, (3-endo)- (CA INDEX NAME)

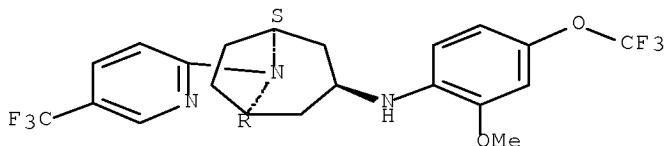
Relative stereochemistry.



RN 933797-69-4 CAPLUS

CN 8-Azabicyclo[3.2.1]octan-3-amine, N-[2-methoxy-4-(trifluoromethoxy)phenyl]-8-[5-(trifluoromethyl)-2-pyridinyl]-, (3-endo)- (CA INDEX NAME)

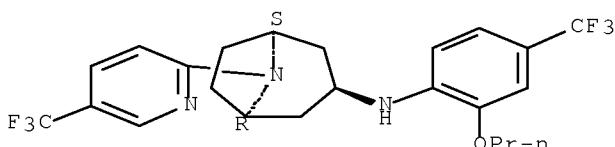
Relative stereochemistry.



RN 933797-70-7 CAPLUS

CN 8-Azabicyclo[3.2.1]octan-3-amine, N-[2-propoxy-4-(trifluoromethyl)phenyl]-8-[5-(trifluoromethyl)-2-pyridinyl]-, (3-exo)- (CA INDEX NAME)

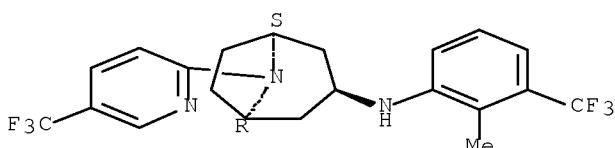
Relative stereochemistry.



RN 933797-71-8 CAPLUS

CN 8-Azabicyclo[3.2.1]octan-3-amine, N-[2-methyl-3-(trifluoromethyl)phenyl]-8-[5-(trifluoromethyl)-2-pyridinyl]-, (3-endo)- (CA INDEX NAME)

Relative stereochemistry.



REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2006:1124114 CAPLUS [Full-text](#)

DOCUMENT NUMBER: 145:455030

TITLE: Preparation of substituted heteroaryl CB<sub>1</sub> antagonists

INVENTOR(S): Yuan, Jun; Guo, Qin; Zhao, He; Hu, Shaojing; Whitehouse, Darren; Fringle, Wallace; Mao, Jianmin; Maynard, George; Hammer, Jack; Wustrow, David; Li, Hongbin

PATENT ASSIGNEE(S): Neurogen Corporation, USA

SOURCE: PCT Int. Appl., 447pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.

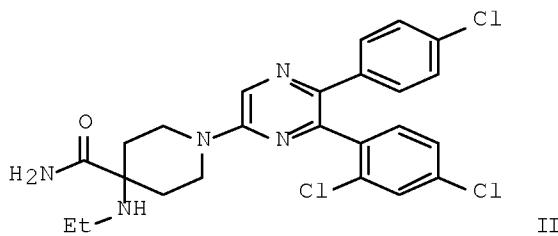
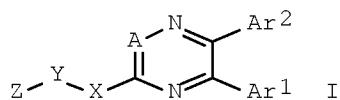
KIND DATE

APPLICATION NO.

DATE

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WO 2006113704 A2 20061026 WO 2006-US14548 20060418  
WO 2006113704 A3 20070208  
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,  
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,  
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR,  
KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX,  
MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE,  
SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC,  
VN, YU, ZA, ZM, ZW  
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,  
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CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,  
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,  
KG, KZ, MD, RU, TJ, TM  
CA 2606288 A1 20061026 CA 2006-2606288 20060418  
US 2007078135 A1 20070405 US 2006-406532 20060418  
EP 1871762 A2 20080102 EP 2006-750555 20060418  
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,  
IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR  
PRIORITY APPLN. INFO.: US 2005-672452P P 20050418  
WO 2006-US14548 W 20060418

OTHER SOURCE(S): MARPAT 145:455030  
GI



AB The title compds. I [A = CR1 or N; Ar1, Ar2 = (un)substituted 5-10 membered carbocycle and heterocycle; X = (un)substituted CH<sub>2</sub>, O, NH or SO<sub>m</sub>NH; m = 0-2; Y = (un)substituted alkylene; Z = (un)substituted OH, NH<sub>2</sub>, SO<sub>m</sub>NH<sub>2</sub>, etc.; R1 = H, halo, CN, etc.] which may be used to modulate CB<sub>1</sub> activity in vivo or in vitro, and are particularly useful in the treatment of conditions responsive to CB<sub>1</sub> modulation in humans, domesticated companion animals and livestock animals, including appetite disorders, obesity and addictive disorders, were prepared E.g., a multi-step synthesis of II, starting from 2,6-dichloropyrazine and 4-(ethylamino)piperidine-4-carboxamide, was given. Exemplified compds. I were tested at CB<sub>1</sub> receptor. Thus, II as many other representative compds. I showed IC<sub>50</sub> of 2 μM or less. Pharmaceutical compns. and methods for using compds. I to treat disorders responsive to CB<sub>1</sub>

modulation are provided, as are methods for using such ligands for receptor localization studies and various in vitro assays.

IT 913281-93-3P 913281-94-4P 913281-97-7P

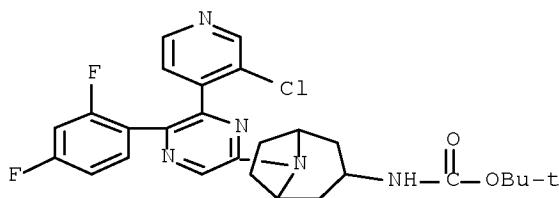
913282-02-7P 913282-12-9P 913282-17-4P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of substituted heteroaryl compds. useful in treatment of diseases responsive to CB1 activation)

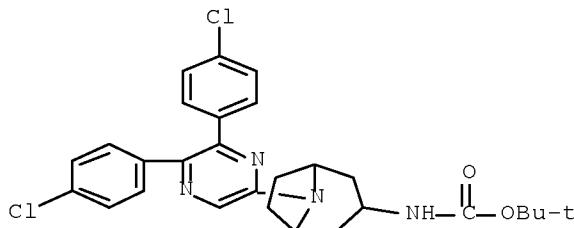
RN 913281-93-3 CAPLUS

CN Carbamic acid, [8-[6-(3-chloro-4-pyridinyl)-5-(2,4-difluorophenyl)pyrazinyl]-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



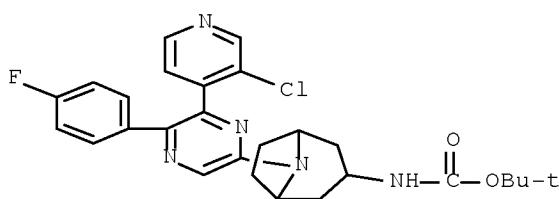
RN 913281-94-4 CAPLUS

CN Carbamic acid, [8-[5,6-bis(4-chlorophenyl)pyrazinyl]-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

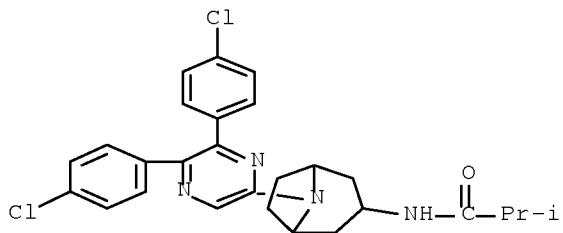


RN 913281-97-7 CAPLUS

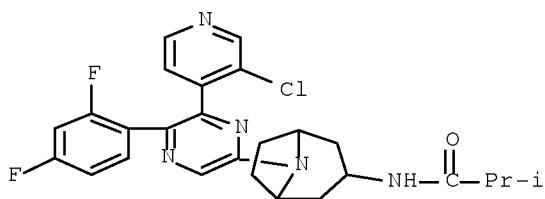
CN Carbamic acid, [8-[6-(3-chloro-4-pyridinyl)-5-(4-fluorophenyl)pyrazinyl]-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



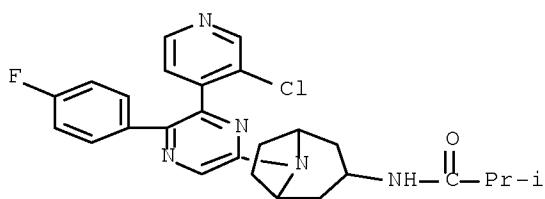
RN 913282-02-7 CAPLUS  
CN Propanamide, N-[8-[5,6-bis(4-chlorophenyl)pyrazinyl]-8-azabicyclo[3.2.1]oct-3-yl]-2-methyl- (9CI) (CA INDEX NAME)



RN 913282-12-9 CAPLUS  
CN Propanamide, N-[8-[6-(3-chloro-4-pyridinyl)-5-(2,4-difluorophenyl)pyrazinyl]-8-azabicyclo[3.2.1]oct-3-yl]-2-methyl- (9CI) (CA INDEX NAME)



RN 913282-17-4 CAPLUS  
CN Propanamide, N-[8-[6-(3-chloro-4-pyridinyl)-5-(4-fluorophenyl)pyrazinyl]-8-azabicyclo[3.2.1]oct-3-yl]-2-methyl- (9CI) (CA INDEX NAME)

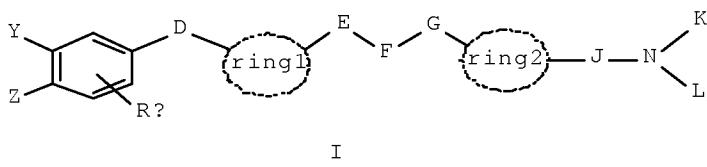


L3 ANSWER 5 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN  
ACCESSION NUMBER: 2006:606621 CAPLUS Full-text  
DOCUMENT NUMBER: 145:63034  
TITLE: Preparation of silicon compounds and their use in

INVENTOR(S): Showell, Graham Andrew; Walsh, Louise Marie; Mandal, Ajay Kumar  
 PATENT ASSIGNEE(S): Paradigm Therapeutics Ltd., UK  
 SOURCE: PCT Int. Appl., 55 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006064277	A1	20060622	WO 2005-GB4905	20051216
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
AU 2005315331	A1	20060622	AU 2005-315331	20051216
CA 2590881	A1	20060622	CA 2005-2590881	20051216
EP 1824863	A1	20070829	EP 2005-820647	20051216
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR				
CN 101107259	A	20080116	CN 2005-80043255	20051216
IN 2007DN03844	A	20070831	IN 2007-DN3844	20070522
KR 2007097468	A	20071004	KR 2007-714460	20070625
PRIORITY APPLN. INFO.:			GB 2004-27722	A 20041217
			WO 2005-GB4905	W 20051216

OTHER SOURCE(S): CASREACT 145:63034; MARPAT 145:63034  
GI



AB Preparation of title compds., e.g. I (D = (un)substituted alkylene, O, thionyl, sulfonyl, etc.; E, F, G = same or different (un)substituted alkylene, (un)substituted amino, etc.; J = bond, heterocycloalkyl, etc.; K, L = same or different H, alkyl, cycloalkyl, alkoxy, etc.; Ra, K or L taken together as heterocycloalkyl; Ra = H, halo, alkyl, aryl, hydroxy, alkoxy, etc.; Y, Z = same or different H, halo, alkyl, hydroxy, alkoxy, cyano, organosilyl, etc.; ring1 and ring2 = same or different arylene, heteroarylene optionally

substituted with Ra; at least one of Y and Z includes a Si atom), and their use in therapy is described.

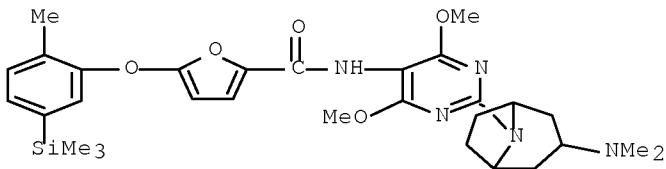
IT 891860-56-3P, 5-(2-Methyl-5-(trimethylsilyl)phenoxy)-N-(2-(3-(dimethylamino)-8-azabicyclo[3.2.1]octan-8-yl)-4,6-dimethoxypyrimidin-5-yl)furan-2-carboxamide

RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of organosilyl compds. and their use in medicament)

RN 891860-56-3 CAPLUS

CN 2-Furancarboxamide, N-[2-[3-(dimethylamino)-8-azabicyclo[3.2.1]oct-8-yl]-4,6-dimethoxy-5-pyrimidinyl]-5-[2-methyl-5-(trimethylsilyl)phenoxy]- (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 6 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2003:1006982 CAPLUS [Full-text](#)

DOCUMENT NUMBER: 140:59518

TITLE: Preparation of [[(8-azabicyclo[3.2.1]octyl)amino]acetyl]- or [[(9-azabicyclo[3.3.1]nonyl)amino]acetyl]heterocyclic carbonitriles as dipeptidyl-peptidase-IV inhibitors

INVENTOR(S): Aranyi, Peter; Balazs, Laszlo; Bata, Imre; Batori, Sandor; Boronkay, Eva; Kapui, Zoltan; Susan, Edit; Szabo, Tibor; Nagy, Lajos T.; Urban-Szabo, Katalin; Varga, Marton

PATENT ASSIGNEE(S): Sanofi-Synthelabo, Fr.

SOURCE: PCT Int. Appl., 49 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

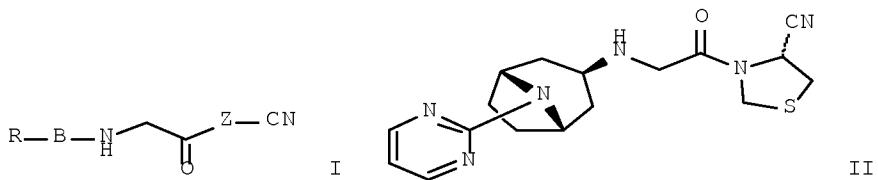
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003106456	A2	20031224	WO 2003-HU41	20030611
WO 2003106456	A3	20040304		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,				

FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,  
 BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG  
 HU 2002002001 A2 20050829 HU 2002-2001 20020614  
 AU 2003244880 A1 20031231 AU 2003-244880 20030611  
 BR 2003011771 A 20050329 BR 2003-11771 20030611  
 EP 1517907 A2 20050330 EP 2003-738355 20030611  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK  
 CN 1662530 A 20050831 CN 2003-813858 20030611  
 JP 2005532369 T 20051027 JP 2004-513288 20030611  
 NZ 537633 A 20060831 NZ 2003-537633 20030611  
 IN 2004KN01852 A 20051230 IN 2004-KN1852 20041206  
 ZA 2004009907 A 20060830 ZA 2004-9907 20041207  
 KR 756761 B1 20070907 KR 2004-720277 20041213  
 MX 2004PA12691 A 20050815 MX 2004-PA12691 20041214  
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 US 2005153973 A1 20050714 US 2005-518114 20050321  
 PRIORITY APPLN. INFO.: HU 2002-2001 A 20020614  
 WO 2003-HU41 W 20030611

OTHER SOURCE(S): MARPAT 140:59518

GI



**AB** Title compds. I [wherein R = (un)substituted N-containing 1- or 2-ring aromatic moieties, p-tolylsulfonyl, R1aCH2, or R1bCO; R1a = H or (un)substituted alkyl, Ph, PhCH2, Ph(CH2)2, PhCH=CH, naphthyl, pyridyl, etc.; R1b = (un)substituted alkyl, Ph, PhCH2, Ph(CH2)2, PhCH=CH, naphthyl, pyridyl, etc.; B = 8-azabicyclo[3.2.1]octyl or 9-azabicyclo[3.3.1]nonyl; Z = thiazolidinediyl, (hydroxy or oxo)pyrrololidinediyl, oxazolidinediyl, or dihydropyrrololidinediyl; and salts, isomers, tautomers, hydrates, or solvates thereof] were prepared as dipeptidyl-peptidase-IV (DPP-IV) inhibitors. These compds. contain tropane building blocks. For example, substitution of tert-Bu 8-benzyl-8-azabicyclo[3.2.1]oct-3-yl-exo-carbamate with 2-chloropyrimidine gave the 8-pyrimidinyl derivative (67%), which was converted to the amine (77%) using TFA. Amidation of (4R)-3-(tert-butoxycarbonyl)thiazolidine-4-carboxylic acid (88%), followed by deprotection (81%), addition of chloroacetyl chloride (75%), and reduction of the amide to the nitrile (43%), gave (4R)-3-(2-chloroacetyl)thiazolidine-4-carbonitrile. Coupling of 8-(2-pyrimidinyl)-8-azabicyclo[3.2.1]oct-3-yl-exo-amine with the nitrile using TEA in MeCN afforded II (53%). Compds. of the invention show low IC50 values for DPP-IV enzyme inhibitory activity in comparison with known compds. and are strong, long-acting enzyme inhibitors (no data). Thus, I and their pharmaceutical compns. are useful for the treatment of DPP-IV related diseases.

**IT** 637018-37-2P 637018-38-3P 637018-39-4P  
 637018-40-7P 637018-41-8P 637018-42-9P  
 637018-43-0P 637018-44-1P 637018-45-2P  
 637018-53-2P 637018-54-3P 637018-55-4P

637018-56-5P 637018-57-6P 637018-58-7P  
637018-59-8P 637018-60-1P 637018-74-7P  
637018-84-9P 637019-04-6P 637019-05-7P  
637330-99-5P 637331-04-5P 637331-18-1P

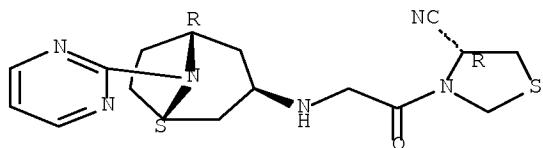
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of [(8-azabicyclo[3.2.1]octyl)amino]acetyl]- or  
[(9-azabicyclo[3.3.1]nonyl)amino]acetyl]heterocyclic carbonitriles as  
DPP-IV inhibitors)

RN 637018-37-2 CAPPLUS

CN 4-Thiazolidinecarbonitrile, 3-[[[(3-exo)-8-(2-pyrimidinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-, (4R)- (9CI) (CA INDEX NAME)

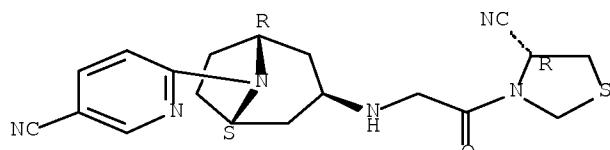
Absolute stereochemistry.



RN 637018-38-3 CAPPLUS

CN 4-Thiazolidinecarbonitrile, 3-[[[(3-exo)-8-(5-cyano-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-, dihydrochloride, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

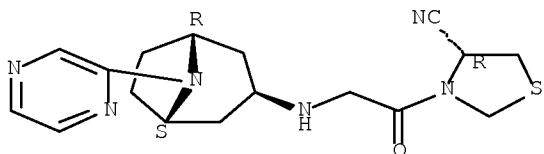


●2 HCl

RN 637018-39-4 CAPPLUS

CN 4-Thiazolidinecarbonitrile, 3-[[[(3-exo)-8-pyrazinyl-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-, dihydrochloride, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

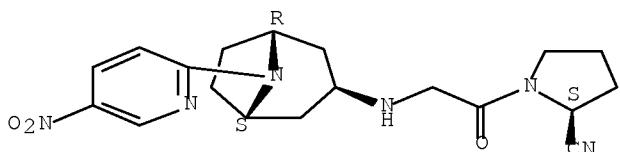


●2 HCl

RN 637018-40-7 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[(3-exo)-8-(5-nitro-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-, (2S)- (9CI) (CA INDEX NAME)

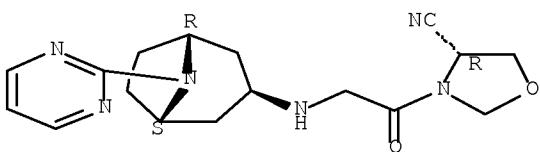
Absolute stereochemistry.



RN 637018-41-8 CAPLUS

CN 4-Oxazolidinecarbonitrile, 3-[[(3-exo)-8-(2-pyrimidinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-, (4R)- (9CI) (CA INDEX NAME)

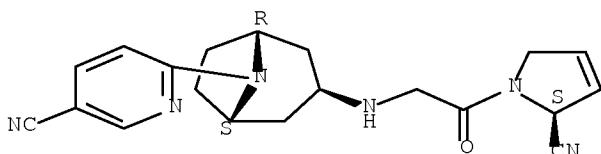
Absolute stereochemistry.



RN 637018-42-9 CAPLUS

CN 1H-Pyrrole-2-carbonitrile, 1-[[(3-exo)-8-(5-cyano-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-2,5-dihydro-, dihydrochloride, (2S)- (9CI) (CA INDEX NAME)

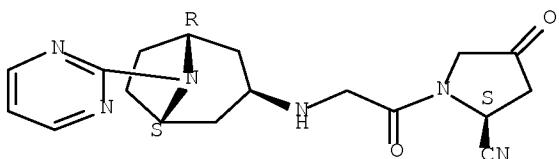
Absolute stereochemistry.



●2 HCl

RN 637018-43-0 CAPLUS  
CN 2-Pyrrolidinecarbonitrile, 4-oxo-1-[[[(3-exo)-8-(2-pyrimidinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-, dihydrochloride, (2S)- (9CI) (CA INDEX NAME)

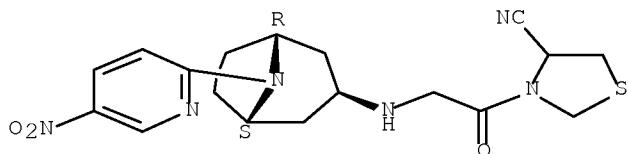
Absolute stereochemistry.



●2 HCl

RN 637018-44-1 CAPLUS  
CN 4-Thiazolidinecarbonitrile, 3-[[[(3-exo)-8-(5-nitro-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-, dihydrochloride (9CI) (CA INDEX NAME)

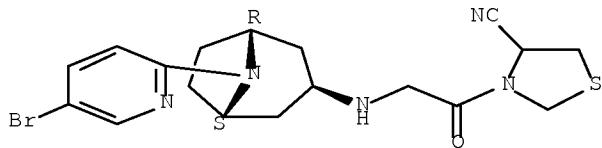
Relative stereochemistry.



●2 HCl

RN 637018-45-2 CAPLUS  
CN 4-Thiazolidinecarbonitrile, 3-[[[(3-exo)-8-(5-bromo-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]- (9CI) (CA INDEX NAME)

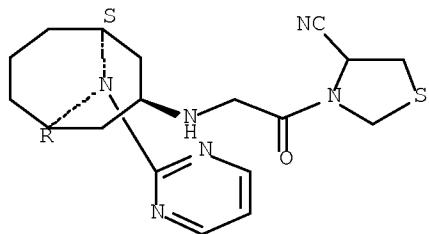
Relative stereochemistry.



RN 637018-53-2 CAPLUS  
CN 4-Thiazolidinecarbonitrile, 3-[[[(3-endo)-9-(2-pyrimidinyl)-9-

azabicyclo[3.3.1]non-3-yl]amino]acetyl]-, dihydrochloride (9CI) (CA INDEX NAME)

Relative stereochemistry.

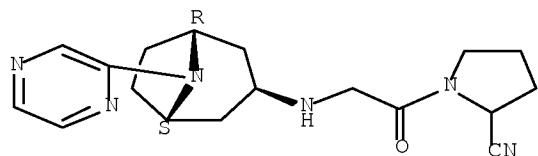


●2 HCl

RN 637018-54-3 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[(3-exo)-8-pyrazinyl-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-, dihydrochloride (9CI) (CA INDEX NAME)

Relative stereochemistry.

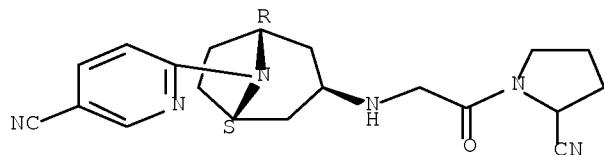


●2 HCl

RN 637018-55-4 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[(3-exo)-8-(5-cyano-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-, dihydrochloride (9CI) (CA INDEX NAME)

Relative stereochemistry.

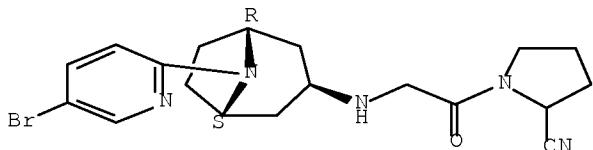


●2 HCl

RN 637018-56-5 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[(3-exo)-8-(5-bromo-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]- (9CI) (CA INDEX NAME)

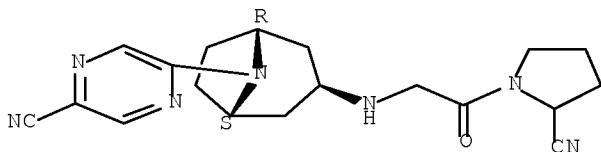
Relative stereochemistry.



RN 637018-57-6 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[(3-exo)-8-(5-cyanopyrazinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]- (9CI) (CA INDEX NAME)

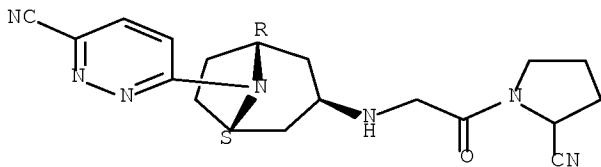
Relative stereochemistry.



RN 637018-58-7 CAPLUS

CN 3-Pyridazinecarbonitrile, 6-[(3-exo)-3-[[2-(2-cyano-1-pyrrolidinyl)-2-oxoethyl]amino]-8-azabicyclo[3.2.1]oct-8-yl]- (CA INDEX NAME)

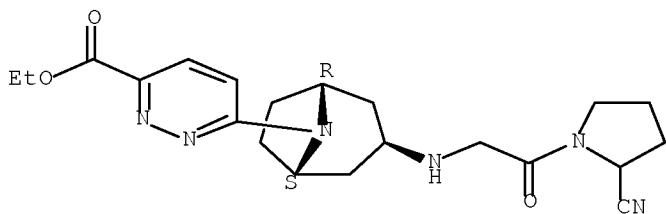
Relative stereochemistry.



RN 637018-59-8 CAPLUS

CN 3-Pyridazinecarboxylic acid, 6-[(3-exo)-3-[[2-(2-cyano-1-pyrrolidinyl)-2-oxoethyl]amino]-8-azabicyclo[3.2.1]oct-8-yl]-, ethyl ester, monohydrochloride (9CI) (CA INDEX NAME)

Relative stereochemistry.

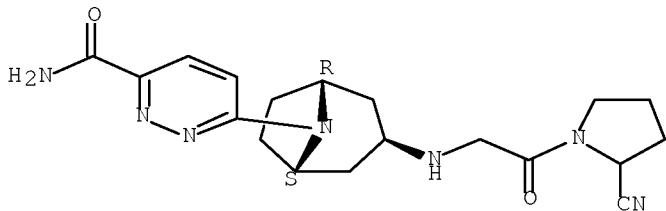


● HCl

RN 637018-60-1 CAPLUS

CN 3-Pyridazinecarboxamide, 6-[(3-exo)-3-[2-(2-cyano-1-pyrrolidinyl)-2-oxoethyl]amino]-8-azabicyclo[3.2.1]oct-8-yl-, monohydrochloride (9CI) (CA INDEX NAME)

Relative stereochemistry.

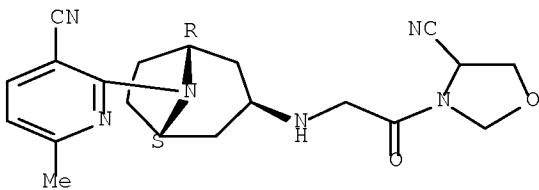


● HCl

RN 637018-74-7 CAPLUS

CN 4-Oxazolidinecarbonitrile, 3-[[[(3-exo)-8-(3-cyano-6-methyl-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-, dihydrochloride (9CI) (CA INDEX NAME)

Relative stereochemistry.

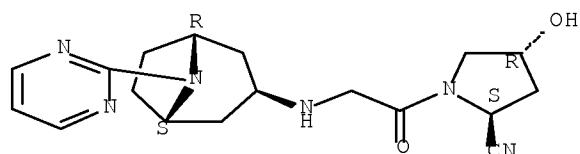


● 2 HCl

RN 637018-84-9 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 4-hydroxy-1-[[[(3-exo)-8-(2-pyrimidinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-, (2S,4R)- (9CI) (CA INDEX NAME)

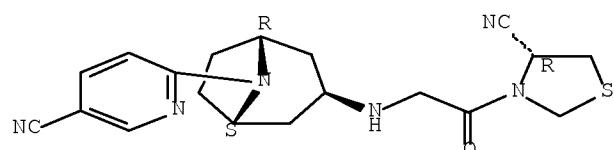
Absolute stereochemistry.



RN 637019-04-6 CAPLUS

CN 4-Thiazolidinecarbonitrile, 3-[[[(3-exo)-8-(5-cyano-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-, (4R)- (9CI) (CA INDEX NAME)

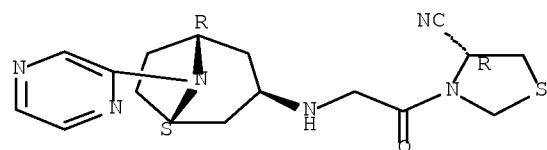
Absolute stereochemistry.



RN 637019-05-7 CAPLUS

CN 4-Thiazolidinecarbonitrile, 3-[[[(3-exo)-8-pyrazinyl-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-, (4R)- (9CI) (CA INDEX NAME)

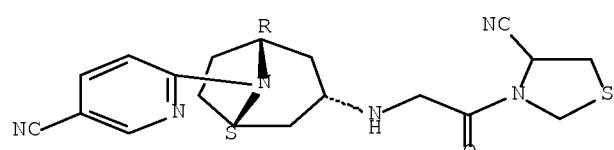
Absolute stereochemistry.



RN 637330-99-5 CAPLUS

CN 4-Thiazolidinecarbonitrile, 3-[[[(3-endo)-8-(5-cyano-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]- (9CI) (CA INDEX NAME)

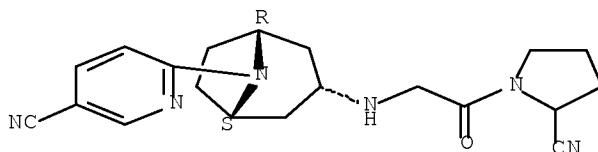
Relative stereochemistry.



RN 637331-04-5 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[(3-endo)-8-(5-cyano-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]- (9CI) (CA INDEX NAME)

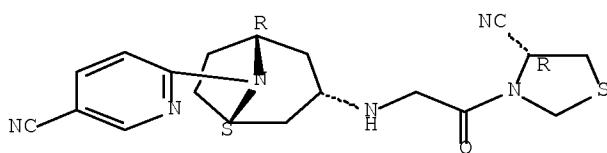
Relative stereochemistry.



RN 637331-18-1 CAPLUS

CN 4-Thiazolidinecarbonitrile, 3-[[[(3-endo)-8-(5-cyano-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-, (4R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 596816-99-8P 596817-00-4P 596817-03-7P  
596817-04-8P 596817-10-6P 596817-11-7P  
596817-14-0P 596817-15-1P 596817-16-2P  
596817-22-0P 596817-37-7P 596817-66-2P  
596817-67-3P 596817-70-8P 596817-71-9P  
596817-72-0P 596817-78-6P 596817-92-4P  
637331-09-0P 637331-13-6P

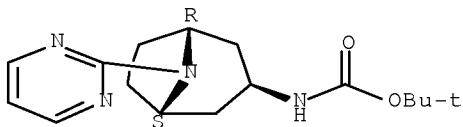
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of [[(8-azabicyclo[3.2.1]octyl)amino]acetyl]- or  
[[9-azabicyclo[3.3.1]nonyl)amino]acetyl]heterocyclic carbonitriles as  
DPP-IV inhibitors)

RN 596816-99-8 CAPLUS

CN Carbamic acid, [(3-exo)-8-(2-pyrimidinyl)-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

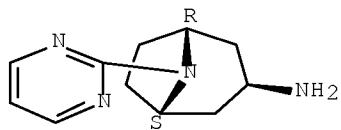
Relative stereochemistry.



RN 596817-00-4 CAPLUS

CN 8-Azabicyclo[3.2.1]octan-3-amine, 8-(2-pyrimidinyl)-, (3-exo)- (CA INDEX NAME)

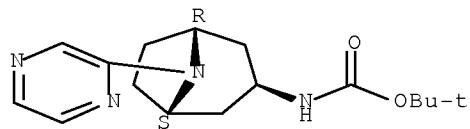
Relative stereochemistry.



RN 596817-03-7 CAPLUS

CN Carbamic acid, [(3-exo)-8-pyrazinyl-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

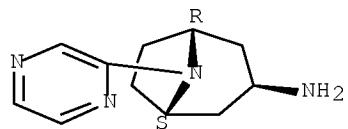
Relative stereochemistry.



RN 596817-04-8 CAPLUS

CN 8-Azabicyclo[3.2.1]octan-3-amine, 8-pyrazinyl-, (3-exo)- (9CI) (CA INDEX NAME)

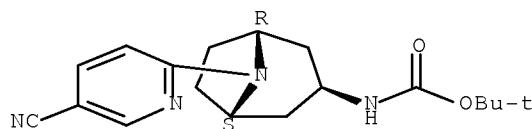
Relative stereochemistry.



RN 596817-10-6 CAPLUS

CN Carbamic acid, [(3-exo)-8-(5-cyano-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

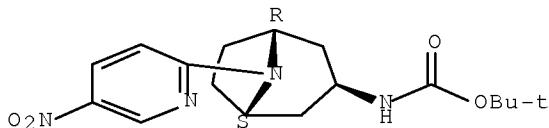
Relative stereochemistry.



RN 596817-11-7 CAPLUS

CN Carbamic acid, [(3-exo)-8-(5-nitro-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

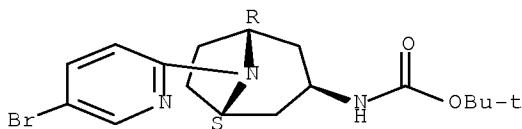
Relative stereochemistry.



RN 596817-14-0 CAPLUS

CN Carbamic acid, [(3-exo)-8-(5-bromo-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

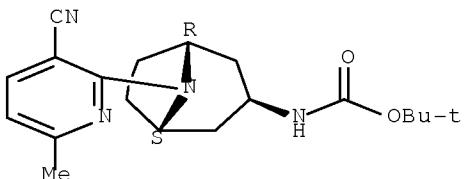
Relative stereochemistry.



RN 596817-15-1 CAPLUS

CN Carbamic acid, [(3-exo)-8-(3-cyano-6-methyl-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

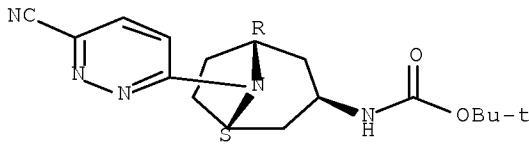
Relative stereochemistry.



RN 596817-16-2 CAPLUS

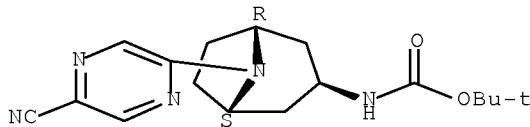
CN Carbamic acid, [(3-exo)-8-(6-cyano-3-pyridazinyl)-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.



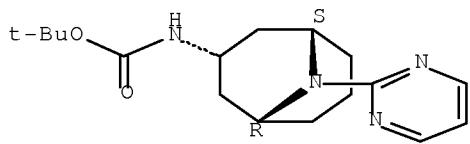
RN 596817-22-0 CAPLUS  
CN Carbamic acid, [(3-exo)-8-(5-cyanopyrazinyl)-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.



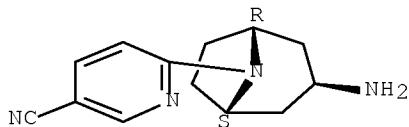
RN 596817-37-7 CAPLUS  
CN Carbamic acid, [(3-endo)-9-(2-pyrimidinyl)-9-azabicyclo[3.3.1]non-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.



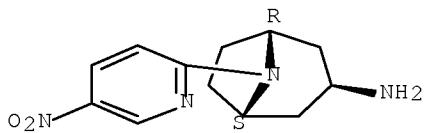
RN 596817-66-2 CAPLUS  
CN 3-Pyridinecarbonitrile, 6-[(3-exo)-3-amino-8-azabicyclo[3.2.1]oct-8-yl]- (CA INDEX NAME)

Relative stereochemistry.



RN 596817-67-3 CAPLUS  
CN 8-Azabicyclo[3.2.1]octan-3-amine, 8-(5-nitro-2-pyridinyl)-, (3-exo)- (CA INDEX NAME)

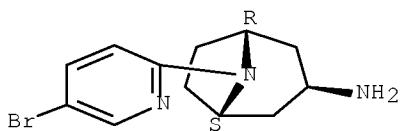
Relative stereochemistry.



RN 596817-70-8 CAPLUS

CN 8-Azabicyclo[3.2.1]octan-3-amine, 8-(5-bromo-2-pyridinyl)-, (3-exo)- (CA INDEX NAME)

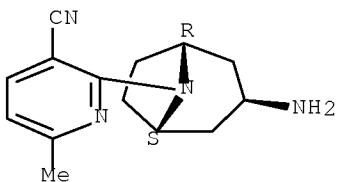
Relative stereochemistry.



RN 596817-71-9 CAPLUS

CN 3-Pyridinecarbonitrile, 2-[(3-exo)-3-amino-8-azabicyclo[3.2.1]oct-8-yl]-6-methyl- (CA INDEX NAME)

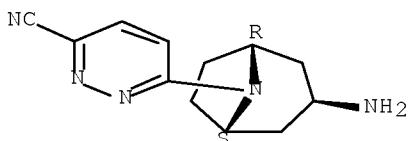
Relative stereochemistry.



RN 596817-72-0 CAPLUS

CN 3-Pyridazinecarbonitrile, 6-[(3-exo)-3-amino-8-azabicyclo[3.2.1]oct-8-yl]- (CA INDEX NAME)

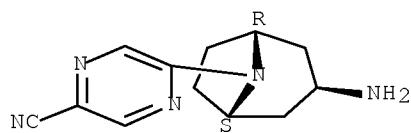
Relative stereochemistry.



RN 596817-78-6 CAPLUS

CN Pyrazinecarbonitrile, 5-[(3-exo)-3-amino-8-azabicyclo[3.2.1]oct-8-yl]- (9CI) (CA INDEX NAME)

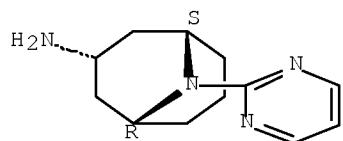
Relative stereochemistry.



RN 596817-92-4 CAPLUS

CN 9-Azabicyclo[3.3.1]nonan-3-amine, 9-(2-pyrimidinyl)-, (3-endo)- (CA INDEX NAME)

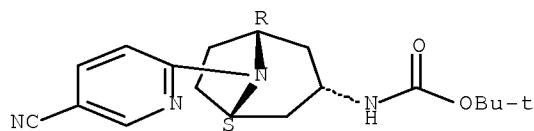
Relative stereochemistry.



RN 637331-09-0 CAPLUS

CN Carbamic acid, [(3-endo)-8-(5-cyano-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

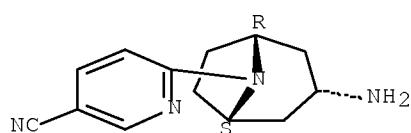
Relative stereochemistry.



RN 637331-13-6 CAPLUS

CN 3-Pyridinecarbonitrile, 6-[(3-endo)-3-amino-8-azabicyclo[3.2.1]oct-8-yl]- (CA INDEX NAME)

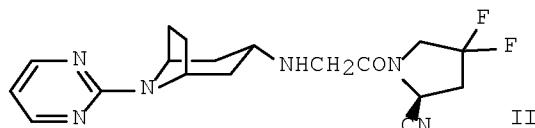
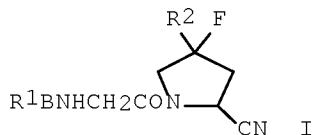
Relative stereochemistry.



L3 ANSWER 7 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 2003:719461 CAPLUS Full-text  
 DOCUMENT NUMBER: 139:245893  
 TITLE: Preparation of aminoacetylpyrrolidinecarbonitriles as  
       inhibitors of DPP-IV  
 INVENTOR(S): Aranyi, Peter; Balazs, Laszlo; Bata, Imre; Batori,  
               Sandor; Boronkay, Eva; Bovy, Philippe; Kanai, Karoly;  
               Kapui, Zoltan; Susan, Edit; Szabo, Tibor; Nagy, Lajos  
               T.; Urban-Szabo, Katalin; Varga, Marton  
 PATENT ASSIGNEE(S): Sanofi-Synthelabo, Fr.; et al.  
 SOURCE: PCT Int. Appl., 53 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003074500	A2	20030912	WO 2003-HU17	20030304
WO 2003074500	A3	20031218		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
HU 2002000849	A2	20040830	HU 2002-849	20020306
CA 2475312	A1	20030912	CA 2003-2475312	20030304
AU 2003209514	A1	20030916	AU 2003-209514	20030304
EP 1487807	A2	20041222	EP 2003-743452	20030304
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BR 2003007960	A	20050215	BR 2003-7960	20030304
CN 1639159	A	20050713	CN 2003-805263	20030304
JP 2005529078	T	20050929	JP 2003-572969	20030304
NZ 535662	A	20070531	NZ 2003-535662	20030304
CN 1990486	A	20070704	CN 2006-10164020	20030304
TW 250978	B	20060311	TW 2003-92104743	20030306
IN 2004KN01079	A	20060127	IN 2004-KN1079	20040728
ZA 2004006467	A	20050622	ZA 2004-6467	20040813
MX 2004PA08613	A	20050608	MX 2004-PA8613	20040906
NO 2004004221	A	20041206	NO 2004-4221	20041005
US 2005130981	A1	20050616	US 2005-507005	20050131
PRIORITY APPLN. INFO.:			HU 2002-849	A 20020306
			CN 2003-805263	A3 20030304
			WO 2003-HU17	W 20030304

OTHER SOURCE(S): MARPAT 139:245893  
 GI



AB Title compds. I [R1 = (un)substituted N heteroarom., thiienyl, furyl, CH<sub>2</sub>Ph, tosyl, acyl; B = N heterocyclic; R2 - H, F] were prepared for use as dipeptidyl peptidase IV (DPP-IV) inhibitors with IC<sub>50</sub> ≤ 100 nM, useful in the treatment of diabetes. Thus, the title compound II was prepared from 8-(2-pyrimidinyl)-8-azabicyclo[3.2.1]oct-3-yl-exo-amine and (2S)-1-chloroacetyl-4,4-difluoro-2-pyrrolidinecarbonitrile, each prepared in several steps.

IT 596816-99-8P 596817-00-4P 596817-03-7P  
 596817-04-8P 596817-09-3P 596817-10-6P  
 596817-11-7P 596817-12-8P 596817-13-9P  
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 596817-70-8P 596817-71-9P 596817-72-0P  
 596817-73-1P 596817-74-2P 596817-75-3P  
 596817-76-4P 596817-77-5P 596817-78-6P  
 596817-79-7P 596817-89-9P 596817-90-2P  
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 599165-29-4P 599165-31-8P 599165-32-9P  
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RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

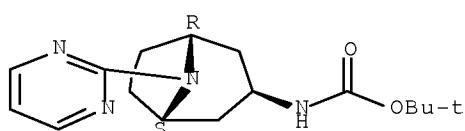
(preparation of aminoacetylpyrrolidinecarbonitriles as inhibitors of DPP-

IV)

RN 596816-99-8 CAPLUS

CN Carbamic acid, [(3-exo)-8-(2-pyrimidinyl)-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.

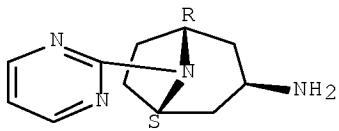


RN 596817-00-4 CAPLUS

CN 8-Azabicyclo[3.2.1]octan-3-amine, 8-(2-pyrimidinyl)-, (3-exo)- (CA INDEX

NAME)

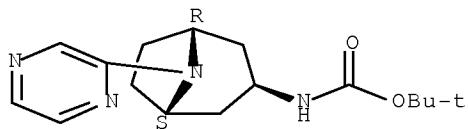
Relative stereochemistry.



RN 596817-03-7 CAPLUS

CN Carbamic acid, [(3-exo)-8-pyrazinyl-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

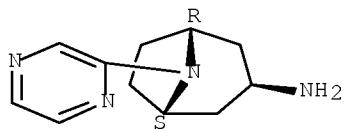
Relative stereochemistry.



RN 596817-04-8 CAPLUS

CN 8-Azabicyclo[3.2.1]octan-3-amine, 8-pyrazinyl-, (3-exo)- (9CI) (CA INDEX NAME)

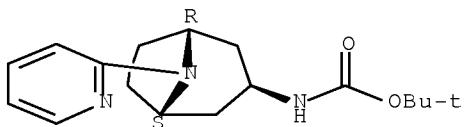
Relative stereochemistry.



RN 596817-09-3 CAPLUS

CN Carbamic acid, [(3-exo)-8-(2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

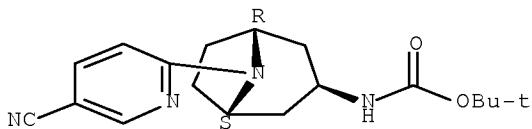
Relative stereochemistry.



RN 596817-10-6 CAPLUS

CN Carbamic acid, [(3-exo)-8-(5-cyano-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

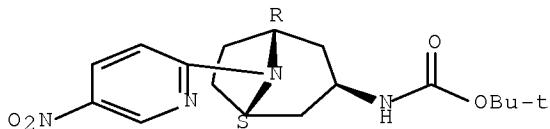
Relative stereochemistry.



RN 596817-11-7 CAPLUS

CN Carbamic acid, [(3-exo)-8-(5-nitro-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

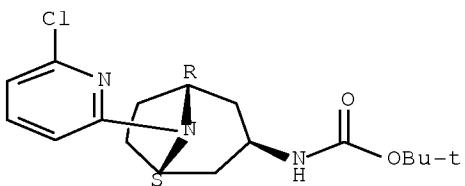
Relative stereochemistry.



RN 596817-12-8 CAPLUS

CN Carbamic acid, [(3-exo)-8-(6-chloro-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

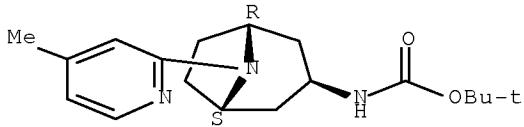
Relative stereochemistry.



RN 596817-13-9 CAPLUS

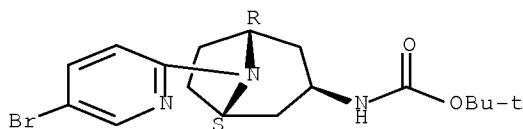
CN Carbamic acid, [(3-exo)-8-(4-methyl-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.



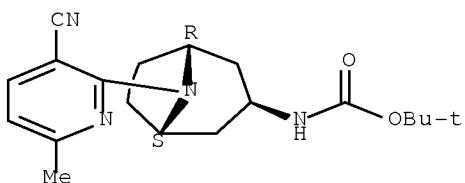
RN 596817-14-0 CAPLUS  
CN Carbamic acid, [(3-exo)-8-(5-bromo-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.



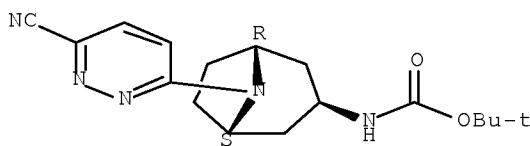
RN 596817-15-1 CAPLUS  
CN Carbamic acid, [(3-exo)-8-(3-cyano-6-methyl-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.



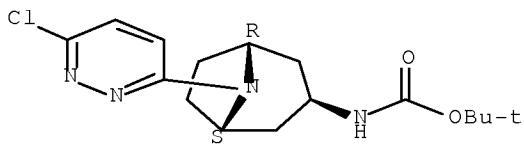
RN 596817-16-2 CAPLUS  
CN Carbamic acid, [(3-exo)-8-(6-cyano-3-pyridazinyl)-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.



RN 596817-17-3 CAPLUS  
CN Carbamic acid, [(3-exo)-8-(6-chloro-3-pyridazinyl)-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

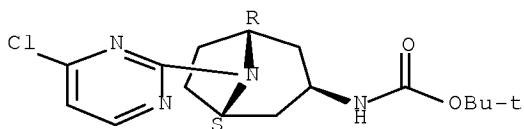
Relative stereochemistry.



RN 596817-18-4 CAPLUS

CN Carbamic acid, [(3-exo)-8-(4-chloro-2-pyrimidinyl)-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

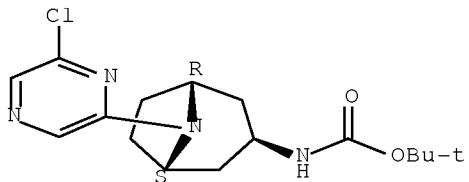
Relative stereochemistry.



RN 596817-19-5 CAPLUS

CN Carbamic acid, [(3-exo)-8-(6-chloropyrazinyl)-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

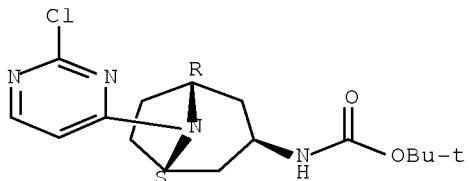
Relative stereochemistry.



RN 596817-20-8 CAPLUS

CN Carbamic acid, [(3-exo)-8-(2-chloro-4-pyrimidinyl)-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.

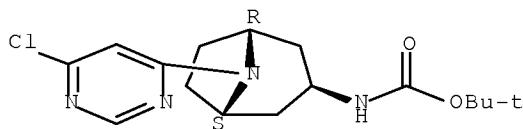


RN 596817-21-9 CAPLUS

CN Carbamic acid, [(3-exo)-8-(6-chloro-4-pyrimidinyl)-8-azabicyclo[3.2.1]oct-

3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

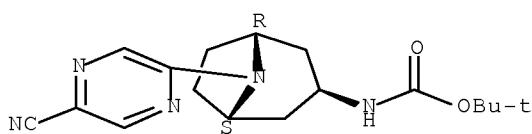
Relative stereochemistry.



RN 596817-22-0 CAPLUS

CN Carbamic acid, [(3-exo)-8-(5-cyanopyrazinyl)-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

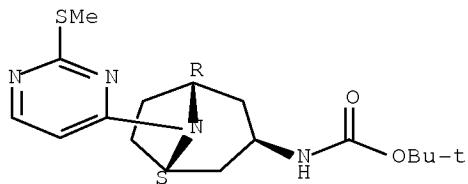
Relative stereochemistry.



RN 596817-23-1 CAPLUS

CN Carbamic acid, [(3-exo)-8-[2-(methylthio)-4-pyrimidinyl]-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

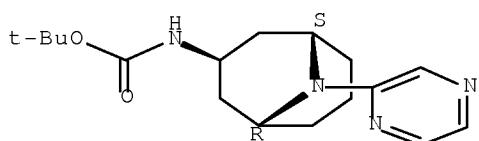
Relative stereochemistry.



RN 596817-34-4 CAPLUS

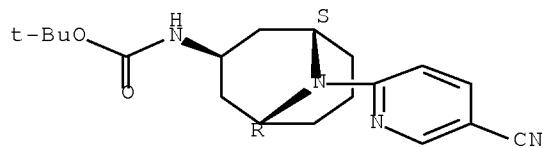
CN Carbamic acid, [(3-exo)-9-pyrazinyl-9-azabicyclo[3.3.1]non-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.



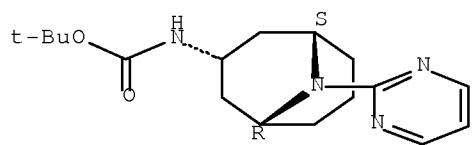
RN 596817-35-5 CAPLUS  
CN Carbamic acid, [(3-exo)-9-(5-cyano-2-pyridinyl)-9-azabicyclo[3.3.1]non-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.



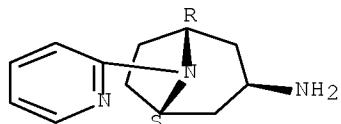
RN 596817-37-7 CAPLUS  
CN Carbamic acid, [(3-endo)-9-(2-pyrimidinyl)-9-azabicyclo[3.3.1]non-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Relative stereochemistry.



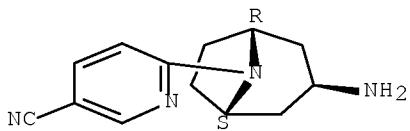
RN 596817-65-1 CAPLUS  
CN 8-Azabicyclo[3.2.1]octan-3-amine, 8-(2-pyridinyl)-, (3-exo)- (CA INDEX NAME)

Relative stereochemistry.



RN 596817-66-2 CAPLUS  
CN 3-Pyridinecarbonitrile, 6-[(3-exo)-3-amino-8-azabicyclo[3.2.1]oct-8-yl]- (CA INDEX NAME)

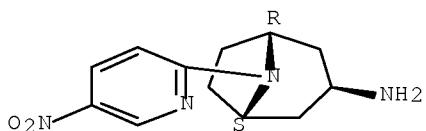
Relative stereochemistry.



RN 596817-67-3 CAPLUS

CN 8-Azabicyclo[3.2.1]octan-3-amine, 8-(5-nitro-2-pyridinyl)-, (3-exo)- (CA INDEX NAME)

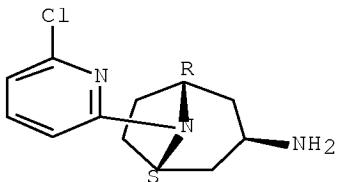
Relative stereochemistry.



RN 596817-68-4 CAPLUS

CN 8-Azabicyclo[3.2.1]octan-3-amine, 8-(6-chloro-2-pyridinyl)-, (3-exo)- (CA INDEX NAME)

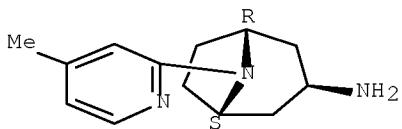
Relative stereochemistry.



RN 596817-69-5 CAPLUS

CN 8-Azabicyclo[3.2.1]octan-3-amine, 8-(4-methyl-2-pyridinyl)-, (3-exo)- (CA INDEX NAME)

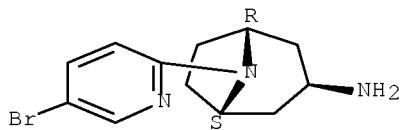
Relative stereochemistry.



RN 596817-70-8 CAPLUS

CN 8-Azabicyclo[3.2.1]octan-3-amine, 8-(5-bromo-2-pyridinyl)-, (3-exo)- (CA INDEX NAME)

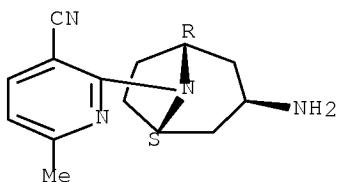
Relative stereochemistry.



RN 596817-71-9 CAPLUS

CN 3-Pyridinecarbonitrile, 2-[ (3-exo)-3-amino-8-azabicyclo[3.2.1]oct-8-yl]-6-methyl- (CA INDEX NAME)

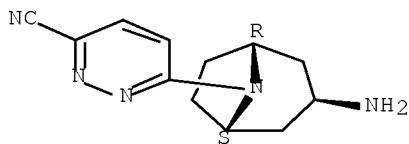
Relative stereochemistry.



RN 596817-72-0 CAPLUS

CN 3-Pyridazinecarbonitrile, 6-[ (3-exo)-3-amino-8-azabicyclo[3.2.1]oct-8-yl]- (CA INDEX NAME)

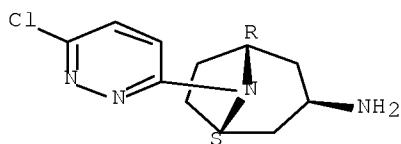
Relative stereochemistry.



RN 596817-73-1 CAPLUS

CN 8-Azabicyclo[3.2.1]octan-3-amine, 8-(6-chloro-3-pyridazinyl)-, (3-exo)- (CA INDEX NAME)

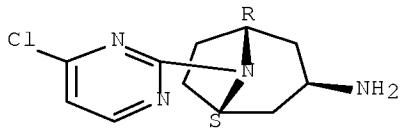
Relative stereochemistry.



RN 596817-74-2 CAPLUS

CN 8-Azabicyclo[3.2.1]octan-3-amine, 8-(4-chloro-2-pyrimidinyl)-, (3-exo)-(CA INDEX NAME)

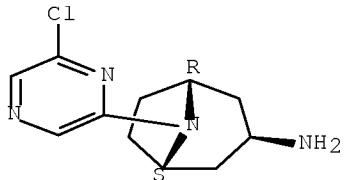
Relative stereochemistry.



RN 596817-75-3 CAPLUS

CN 8-Azabicyclo[3.2.1]octan-3-amine, 8-(6-chloropyrazinyl)-, (3-exo)-(9CI)(CA INDEX NAME)

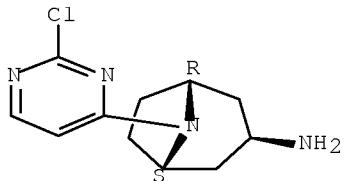
Relative stereochemistry.



RN 596817-76-4 CAPLUS

CN 8-Azabicyclo[3.2.1]octan-3-amine, 8-(2-chloro-4-pyrimidinyl)-, (3-exo)-(CA INDEX NAME)

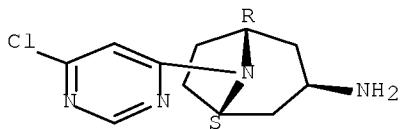
Relative stereochemistry.



RN 596817-77-5 CAPLUS

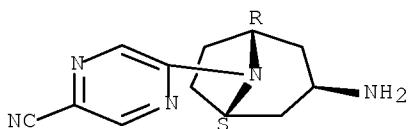
CN 8-Azabicyclo[3.2.1]octan-3-amine, 8-(6-chloro-4-pyrimidinyl)-, (3-exo)-(CA INDEX NAME)

Relative stereochemistry.



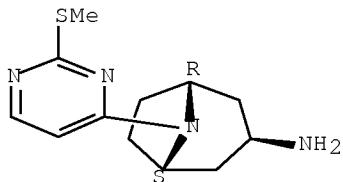
RN 596817-78-6 CAPLUS  
 CN Pyrazinecarbonitrile, 5-[(3-exo)-3-amino-8-azabicyclo[3.2.1]oct-8-yl]-  
 (9CI) (CA INDEX NAME)

Relative stereochemistry.



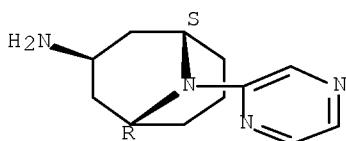
RN 596817-79-7 CAPLUS  
 CN 8-Azabicyclo[3.2.1]octan-3-amine, 8-[2-(methylthio)-4-pyrimidinyl]-,  
 (3-exo)- (CA INDEX NAME)

Relative stereochemistry.



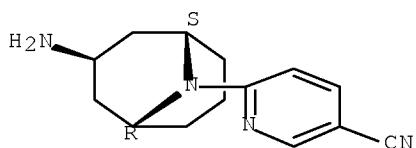
RN 596817-89-9 CAPLUS  
 CN 9-Azabicyclo[3.3.1]nonan-3-amine, 9-pyrazinyl-, (3-exo)- (9CI) (CA INDEX  
 NAME)

Relative stereochemistry.



RN 596817-90-2 CAPLUS  
 CN 3-Pyridinecarbonitrile, 6-[(3-exo)-3-amino-9-azabicyclo[3.3.1]non-9-yl]-  
 (9CI) (CA INDEX NAME)

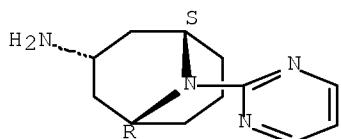
Relative stereochemistry.



RN 596817-92-4 CAPLUS

CN 9-Azabicyclo[3.3.1]nonan-3-amine, 9-(2-pyrimidinyl)-, (3-endo)- (CA INDEX NAME)

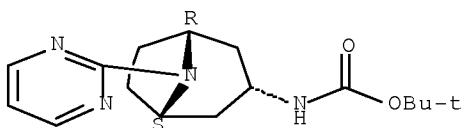
Relative stereochemistry.



RN 599165-27-2 CAPLUS

CN Carbamic acid, [(3-endo)-8-(2-pyrimidinyl)-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

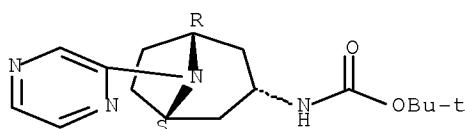
Relative stereochemistry.



RN 599165-28-3 CAPLUS

CN Carbamic acid, [(3-endo)-8-pyrazinyl-8-azabicyclo[3.2.1]oct-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

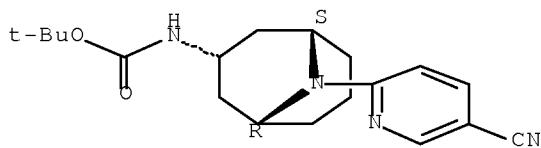
Relative stereochemistry.



RN 599165-29-4 CAPLUS

CN Carbamic acid, [(3-endo)-9-(5-cyano-2-pyridinyl)-9-azabicyclo[3.3.1]non-3-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

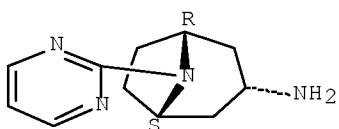
Relative stereochemistry.



RN 599165-31-8 CAPLUS

CN 8-Azabicyclo[3.2.1]octan-3-amine, 8-(2-pyrimidinyl)-, (3-endo)- (CA INDEX NAME)

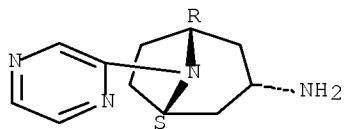
Relative stereochemistry.



RN 599165-32-9 CAPLUS

CN 8-Azabicyclo[3.2.1]octan-3-amine, 8-pyrazinyl-, (3-endo)- (9CI) (CA INDEX NAME)

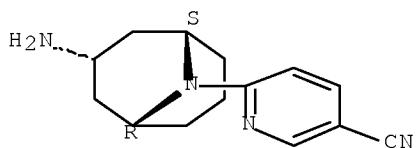
Relative stereochemistry.



RN 599165-33-0 CAPLUS

CN 3-Pyridinecarbonitrile, 6-[(3-endo)-3-amino-9-azabicyclo[3.3.1]non-9-yl]- (9CI) (CA INDEX NAME)

Relative stereochemistry.



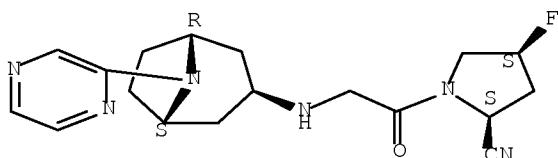
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 596816-28-3P 596816-29-4P 596816-30-7P  
 596816-31-8P 596816-32-9P 596816-33-0P  
 596816-34-1P 596816-35-2P 596816-36-3P  
 596816-37-4P 596816-38-5P 596816-39-6P  
 596816-40-9P 596816-41-0P 596816-51-2P  
 596816-52-3P 596816-53-4P 596816-56-7P  
 596818-14-3P 599165-24-9P 599165-25-0P  
 599165-36-3P  
 RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (preparation of aminoacetylpyrrolidinecarbonitriles as inhibitors of DPP-

IV)

RN 596816-23-8 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[[(3-exo)-8-pyrazinyl-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-, dihydrochloride, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

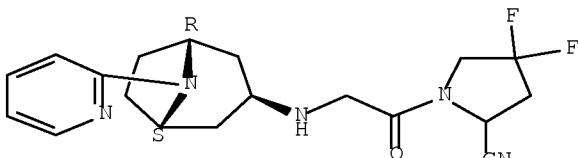


●2 HCl

RN 596816-26-1 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[(3-exo)-8-(2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-, dihydrochloride (9CI) (CA INDEX NAME)

Relative stereochemistry.

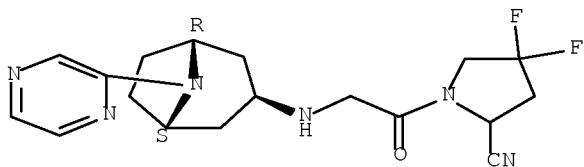


●2 HCl

RN 596816-27-2 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[(3-exo)-8-pyrazinyl-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-, dihydrochloride (9CI) (CA INDEX NAME)

Relative stereochemistry.

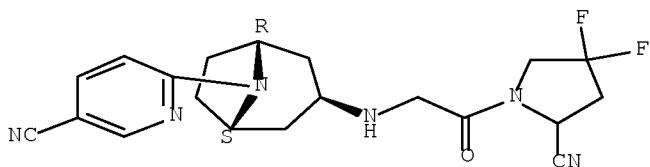


●2 HCl

RN 596816-28-3 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[(3-exo)-8-(5-cyano-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-4,4-difluoro-, dihydrochloride (9CI) (CA INDEX NAME)

Relative stereochemistry.

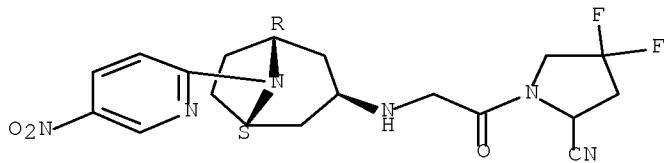


●2 HCl

RN 596816-29-4 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[(3-exo)-8-(5-nitro-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]- (9CI) (CA INDEX NAME)

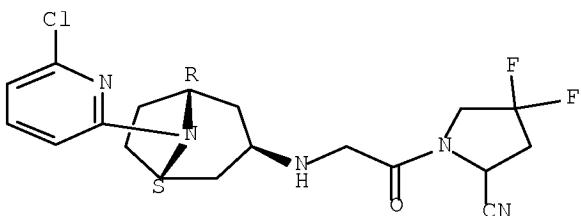
Relative stereochemistry.



RN 596816-30-7 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[(3-exo)-8-(6-chloro-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-4,4-difluoro-, dihydrochloride (9CI) (CA INDEX NAME)

Relative stereochemistry.

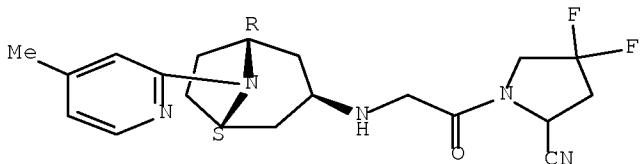


●2 HCl

RN 596816-31-8 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[(3-exo)-8-(4-methyl-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl-, trihydrochloride (9CI) (CA INDEX NAME)

Relative stereochemistry.

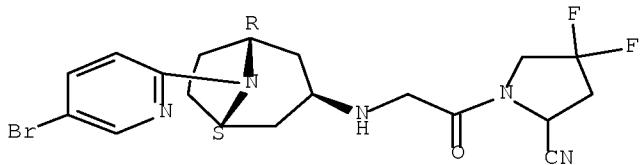


●3 HCl

RN 596816-32-9 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[(3-exo)-8-(5-bromo-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-4,4-difluoro-, dihydrochloride (9CI) (CA INDEX NAME)

Relative stereochemistry.

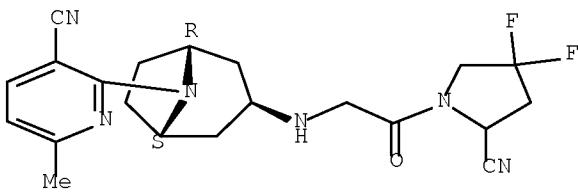


●2 HCl

RN 596816-33-0 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[(3-exo)-8-(3-cyano-6-methyl-2-pyridinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-4,4-difluoro-, dihydrochloride (9CI) (CA INDEX NAME)

Relative stereochemistry.

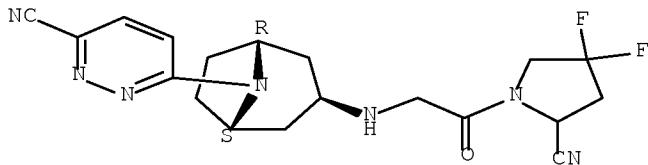


●2 HCl

RN 596816-34-1 CAPLUS

CN 3-Pyridazinecarbonitrile, 6-[(3-exo)-3-[(2-(2-cyano-4,4-difluoro-1-pyrrolidinyl)-2-oxoethyl)amino]-8-azabicyclo[3.2.1]oct-8-yl]- (CA INDEX NAME)

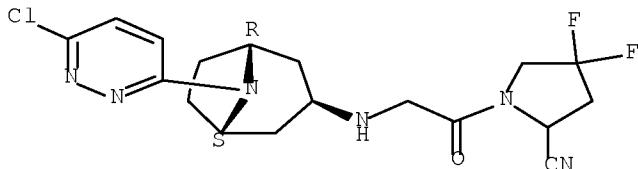
Relative stereochemistry.



RN 596816-35-2 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[(3-exo)-8-(6-chloro-3-pyridazinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-4,4-difluoro-, dihydrochloride (9CI) (CA INDEX NAME)

Relative stereochemistry.

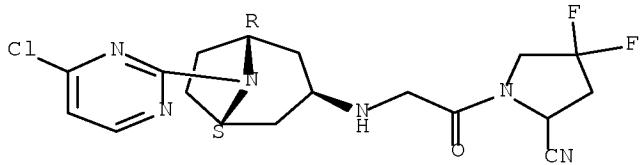


●2 HCl

RN 596816-36-3 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[(3-exo)-8-(4-chloro-2-pyrimidinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-4,4-difluoro-, dihydrochloride (9CI) (CA INDEX NAME)

Relative stereochemistry.

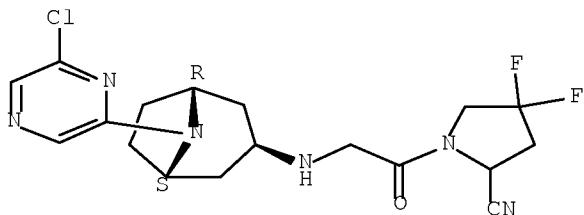


●2 HCl

RN 596816-37-4 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[(3-exo)-8-(6-chloropyrazinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-4,4-difluoro-, dihydrochloride (9CI) (CA INDEX NAME)

Relative stereochemistry.

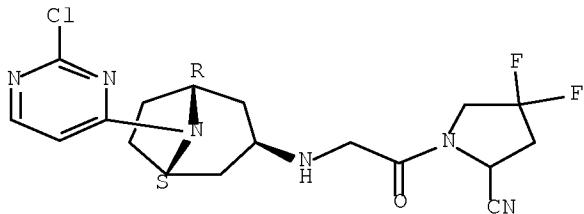


●2 HCl

RN 596816-38-5 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[(3-exo)-8-(2-chloro-4-pyrimidinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-4,4-difluoro-, dihydrochloride (9CI) (CA INDEX NAME)

Relative stereochemistry.

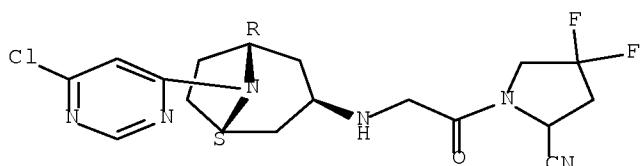


●2 HCl

RN 596816-39-6 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[[(3-exo)-8-(6-chloro-4-pyrimidinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-4,4-difluoro-, dihydrochloride (9CI) (CA INDEX NAME)

Relative stereochemistry.

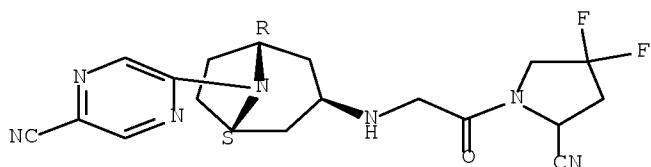


●2 HCl

RN 596816-40-9 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[(3-exo)-8-(5-cyanopyrazinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-4,4-difluoro-, hydrochloride (2:3) (9CI) (CA INDEX NAME)

Relative stereochemistry.

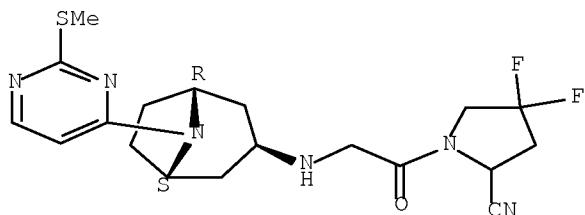


●3/2 HCl

RN 596816-41-0 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[(3-exo)-8-[2-(methylthio)-4-pyrimidinyl]-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl-, dihydrochloride (9CI) (CA INDEX NAME)

Relative stereochemistry.

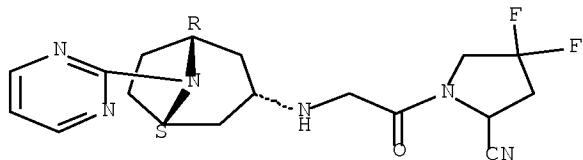


●2 HCl

RN 596816-51-2 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[(3-endo)-8-(2-pyrimidinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl-, (9CI) (CA INDEX NAME)

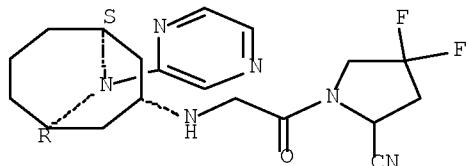
Relative stereochemistry.



RN 596816-52-3 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[(3-exo)-9-pyrazinyl-9-azabicyclo[3.3.1]non-3-yl]amino]acetyl-, dihydrochloride (9CI) (CA INDEX NAME)

Relative stereochemistry.

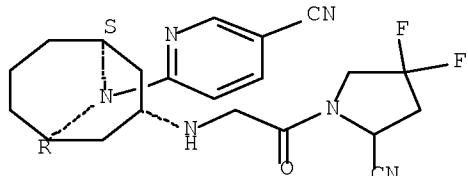


●2 HCl

RN 596816-53-4 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[(3-exo)-9-(5-cyano-2-pyridinyl)-9-azabicyclo[3.3.1]non-3-yl]amino]acetyl]-4,4-difluoro-, dihydrochloride (9CI) (CA INDEX NAME)

Relative stereochemistry.

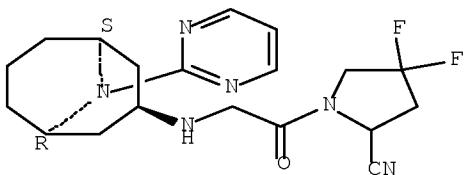


●2 HCl

RN 596816-56-7 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[(3-endo)-9-(2-pyrimidinyl)-9-azabicyclo[3.3.1]non-3-yl]amino]acetyl-, (9CI) (CA INDEX NAME)

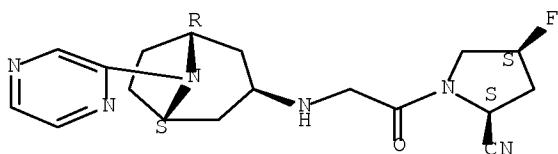
Relative stereochemistry.



RN 596818-14-3 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 4-fluoro-1-[[(3-exo)-8-pyrazinyl-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl-, (2S,4S)- (9CI) (CA INDEX NAME)

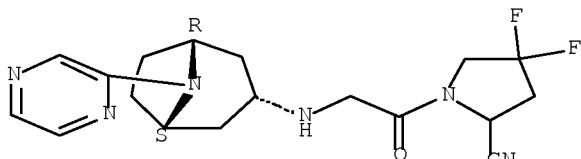
Absolute stereochemistry.



RN 599165-24-9 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[(3-endo)-8-pyrazinyl-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl-, trihydrochloride (9CI) (CA INDEX NAME)

Relative stereochemistry.

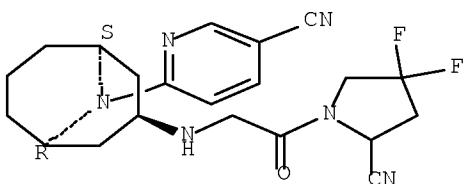


●3 HCl

RN 599165-25-0 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 1-[[(3-endo)-9-(5-cyano-2-pyridinyl)-9-azabicyclo[3.3.1]non-3-yl]amino]acetyl]-4,4-difluoro-, dihydrochloride (9CI) (CA INDEX NAME)

Relative stereochemistry.

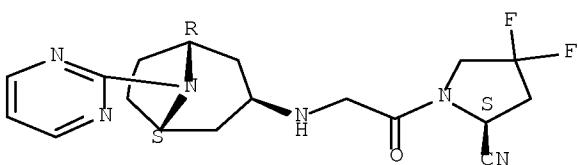


●2 HCl

RN 599165-36-3 CAPLUS

CN 2-Pyrrolidinecarbonitrile, 4,4-difluoro-1-[[[(3-exo)-8-(2-pyrimidinyl)-8-azabicyclo[3.2.1]oct-3-yl]amino]acetyl]-, (2S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L3 ANSWER 8 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 2002:964330 CAPLUS Full-text

DOCUMENT NUMBER: 138:39295

TITLE: Preparation of heterocyclic compounds as Rho-kinase inhibitors

INVENTOR(S): Imazaki, Naonori; Kitano, Masafumi; Ohashi, Naohito; Matsui, Kazuki

PATENT ASSIGNEE(S): Sumitomo Pharmaceuticals Company, Limited, Japan

SOURCE: PCT Int. Appl., 425 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

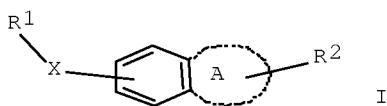
LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002100833	A1	20021219	WO 2002-JP5609	20020606
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2002306284	A1	20021223	AU 2002-306284	20020606
EP 1403255	A1	20040331	EP 2002-733352	20020606

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR  
 US 2004138286 A1 20040715 US 2003-480526 20031212  
 US 7199147 B2 20070403  
 PRIORITY APPLN. INFO.: JP 2001-176826 A 20010612  
 JP 2001-398992 A 20011228  
 WO 2002-JP5609 W 20020606  
 OTHER SOURCE(S): MARPAT 138:39295  
 GI

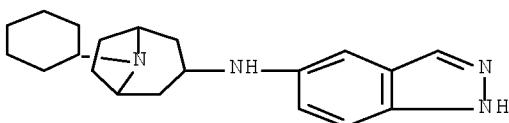


AB The title compds. I [wherein one to four groups represented by the general formula R1-X are present and may be the same or different from each other; A is a saturated or unsatd. five-membered heterocycle; X is a single bond, N(R3), O, S, or the like; R1 is hydrogen, halogeno, nitro, carboxyl, substituted or unsubstituted alkyl, or the like; R2 is hydrogen, halogeno, nitro, carboxyl, substituted or unsubstituted alkyl, or the like; and R3 is hydrogen, substituted or unsubstituted alkyl, or the like] are prepared N-(1-Benzyl-4-piperidinyl)-1H-indazole-5-amine dihydrochloride monohydrate in vitro showed IC50 of 0.4 µL/mL against Rho-kinase.

IT 478837-97-7P  
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (preparation of heterocyclic compds. as Rho-kinase inhibitors)

RN 478837-97-7 CAPLUS

CN 8-Azabicyclo[3.2.1]octan-3-amine, 8-cyclohexyl-N-1H-indazol-5-yl- (CA INDEX NAME)



REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 9 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 2001:827020 CAPLUS Full-text  
 DOCUMENT NUMBER: 136:294764  
 TITLE: Synthesis of 2-(2,3-dimethoxyphenyl)-4-(aminomethyl)imidazole analogues and their binding affinities for dopamine D2 and D3 receptors  
 AUTHOR(S): Huang, Yunsheng; Luedtke, Robert R.; Freeman, Rebekah A.; Wu, Li; Mach, Robert H.

CORPORATE SOURCE: Department of Radiology-PET Center, Wake Forest University School of Medicine, Winston-Salem, NC, 27157, USA

SOURCE: Bioorganic & Medicinal Chemistry (2001), 9(12), 3113-3122

CODEN: BMECEP; ISSN: 0968-0896

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 136:294764

AB A series of 2-(2,3-dimethoxyphenyl)-4-(aminomethyl)imidazole derivs. was prepared and their affinity for dopamine D<sub>2</sub> and D<sub>3</sub> receptors was measured using *in vitro* binding assays. Several oxadiazole analogs were also prepared and tested for their affinity for dopamine D<sub>2</sub> and D<sub>3</sub> receptors. The results of receptor binding studies indicated that the incorporation of an imidazole moiety between the Ph ring and the basic nitrogen did not significantly increase the selectivity for dopamine D<sub>3</sub> receptors, whereas the incorporation of an oxadiazole at the same region resulted in a total loss of affinity for both dopamine receptor subtype binding sites. The most selective compound in this series is 6,7-dimethoxy-2-[2-(2,3-dimethoxyphenyl)-1H-imidazol-4-yl]methyl]-1,2,3,4-tetrahydroisoquinoline, which has a D<sub>3</sub> receptor affinity of 21 nM and a 7-fold selectivity for D<sub>3</sub> vs. D<sub>2</sub> receptors. The binding affinity for σ<sub>1</sub> and σ<sub>2</sub> receptors was also measured, and the results showed that several analogs were selective σ<sub>1</sub> receptor ligands.

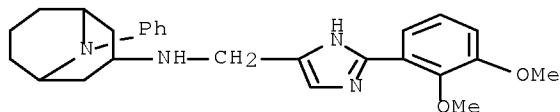
IT 407610-27-9P 407610-28-0P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(preparation and dopamine D<sub>2</sub> and D<sub>3</sub> receptor affinity of 2-(2,3-dimethoxyphenyl)-1H-imidazole-4-methanamine derivs.)

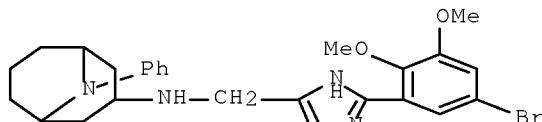
RN 407610-27-9 CAPLUS

CN 9-Azabicyclo[3.3.1]nonan-3-amine, N-[2-(2,3-dimethoxyphenyl)-1H-imidazol-4-yl]methyl]-9-phenyl- (9CI) (CA INDEX NAME)



RN 407610-28-0 CAPLUS

CN 9-Azabicyclo[3.3.1]nonan-3-amine, N-[2-(5-bromo-2,3-dimethoxyphenyl)-1H-imidazol-4-yl]methyl]-9-phenyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT:

28

THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 10 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN  
ACCESSION NUMBER: 2001:229244 CAPLUS Full-text  
DOCUMENT NUMBER: 135:13871  
TITLE: Synthesis and structure-activity relationships of naphthamides as dopamine D3 receptor ligands  
AUTHOR(S): Huang, Yunsheng; Luedtke, Robert R.; Freeman, Rebekah A.; Wu, Li; Mach, Robert H.  
CORPORATE SOURCE: Department of Radiology-PET Center and Department of Physiology Pharmacology, Wake Forest University School of Medicine, Winston-Salem, NC, 27157, USA  
SOURCE: Journal of Medicinal Chemistry (2001), 44(11), 1815-1826  
CODEN: JMCMAR; ISSN: 0022-2623  
PUBLISHER: American Chemical Society  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
OTHER SOURCE(S): CASREACT 135:13871

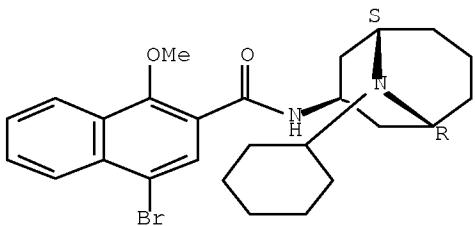
AB A series of naphthamides were synthesized, and the affinities of these compds. were determined for dopamine D2 and D3 receptors using radioligand binding techniques. The naphthamide compds. that were prepared include N-(1-alkylpiperidin-4-yl)-4-bromo-1-methoxy-2-naphthamides (1-6), (S)-N-(1-alkylpyrrolidin-3-yl)-4-bromo-1-methoxy-2-naphthamides (7-12), (R)-N-(1-alkylpyrrolidin-3-yl)-4-bromo-1-methoxy-2-naphthamides (13-18), (S)-N-(1-alkyl-2-pyrrolidinylmethyl)-4-bromo-1-methoxy-2-naphthamides (19-25), (R)-N-(1-alkyl-2-pyrrolidinylmethyl)-4-bromo-1-methoxy-2-naphthamides (26-31), and N-(9-alkyl-9-azabicyclo[3.3.1]nonan-3 $\beta$ -yl)-4-bromo-1-methoxy-2-naphthamides (32, 33). The results of in vitro radioligand binding studies indicated that the majority of the naphthamide analogs bound with high affinity at both the D2 and D3 dopamine receptor subtypes and most of the compds. demonstrated some selectivity for the dopamine D3 dopamine receptor subtype. These results demonstrated that both the structure of the central amine moiety (piperidine, pyrrolidine, and 9-azabicyclo[3.3.1]nonane) ring and the N-(alkyl) substitution on the amine significantly effects the binding affinity at D2 and D3 dopamine receptors. The bulkiness of the N-(1-alkyl) substituent was found to (a) have no effect on pharmacol. selectivity, (b) increase the affinity at D3 receptors, or (c) decrease the affinity at D2 receptors. The most potent analog in this series was (S)-N-(1-cycloheptylpyrrolidin-3-yl)-4-bromo-1-methoxy-2-naphthamide (10), which had equilibrium dissociation (Ki) values of 1.8 and 0.2 nM for D2 and D3 receptors, resp. The most selective analog was (R)-N-(1-cycloheptyl-2-pyrrolidinylmethyl)-4-bromo-1-methoxy-2-naphthamide (30), which had Ki values of 62.8 and 2.4 nM for D2 and D3 receptors, resp. Radioligand binding results for  $\sigma$  receptors indicated that the structure of the amine moiety and the N-(1-alkyl) substitutions also significantly influence the affinity and selectivity of these compds. at the  $\sigma_1$  and  $\sigma_2$  sigma receptor subtypes. The two naphthamides containing a 9-azabicyclo[3.3.1]nonan-3 $\beta$ -yl central ring were found to be selective for  $\sigma_2$  receptors.

IT 342876-79-3P  
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)  
(design and SAR of naphthamides as dopamine D3 receptor ligands)

RN 342876-79-3 CAPLUS

CN 2-Naphthalenecarboxamide, 4-bromo-N-[ (3-exo)-9-cyclohexyl-9-azabicyclo[3.3.1]non-3-yl]-1-methoxy- (CA INDEX NAME)

Relative stereochemistry.



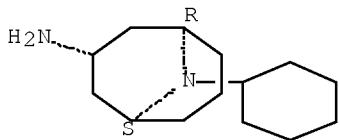
IT 342876-83-9P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(design and SAR of naphthamides as dopamine D3 receptor ligands)

RN 342876-83-9 CAPLUS

CN 9-Azabicyclo[3.3.1]nonan-3-amine, 9-cyclohexyl-, (3-exo)- (CA INDEX NAME)

Relative stereochemistry.



REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 11 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1993:101950 CAPLUS Full-text

DOCUMENT NUMBER: 118:101950

TITLE: Preparation of pyrazolo[1,5-a]pyridine derivatives as serotonin 3 (5-HT3) antagonists

INVENTOR(S): Ito, Yasuo; Kato, Hideo; Yasuda, Shingo; Iwasaki, Nobuhiko; Nishino, Hiroyuki

PATENT ASSIGNEE(S): Hokuriku Pharmaceutical Co., Ltd., Japan

SOURCE: Jpn. Kokai Tokkyo Koho, 5 pp.

CODEN: JKXXAF

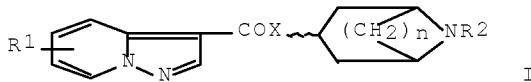
DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 04257591	A	19920911	JP 1991-37776	19910208
PRIORITY APPLN. INFO.:			JP 1991-37776	19910208
OTHER SOURCE(S):	MARPAT	118:101950		
GI				



AB The title derivs. I ( $R_1 = H$ , lower alkyl;  $R_2 = H$ ,  $\text{PhCH}_2$ , lower alkyl;  $X = \text{NH}, O$ ;  $n = 2, 3$ ) or their pharmaceutically acceptable salts are prepared as 5-HT<sub>3</sub> antagonists (no data). Chlorination of 1.00 g pyrazolo[1,5-a]pyridine-3-carboxylic acid in  $\text{CH}_2\text{Cl}_2$  gave pyrazolo[1,5-a]pyridine-3-carbonyl chloride, which in  $\text{CH}_2\text{Cl}_2$  was added dropwise into a mixture of 0.95 g exo-8-methyl-8-azabicyclo[3.3.1]octan-3-amine and Et<sub>3</sub>N in  $\text{CH}_2\text{Cl}_2$  under ice cooling, then stirred at room temperature for 1.5 h to give 0.88 g exo-N-(8-methyl-8-azabicyclo[3.3.1]oct-3-yl)pyrazolo[1,5-a]pyridine-3-carboxamide.

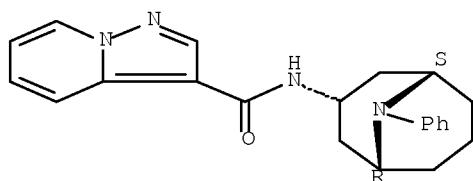
IT 145663-01-0P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of, as 5-HT<sub>3</sub> antagonist)

RN 145663-01-0 CAPLUS

CN Pyrazolo[1,5-a]pyridine-3-carboxamide, N-(9-phenyl-9-azabicyclo[3.3.1]non-3-yl)-, endo- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L3 ANSWER 12 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1984:510862 CAPLUS Full-text

DOCUMENT NUMBER: 101:110862

ORIGINAL REFERENCE NO.: 101:16933a, 16936a

TITLE: Studies on the neuroleptic benzamides. III.  
Synthesis and antidopaminergic properties of new  
3-nortropane derivatives

AUTHOR(S): Dostert, Philippe; Imbert, Thierry; Langlois, Michel;  
Bucher, Bernard; Mocquet, Gisele

CORPORATE SOURCE: Cent. Rech., Rueil-Malmaison, 92500, Fr.

SOURCE: European Journal of Medicinal Chemistry (1984), 19(2),  
105-10

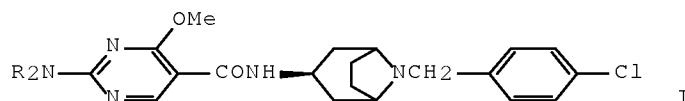
CODEN: EJMCA5; ISSN: 0009-4374

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 101:110862

GI



AB Pyrimidinecarboxamides were prepared from 4-alkoxypyrimidine-5-carboxylic acids and 3-aminonortropane derivs. and were tested for their potential antipsychotic activity. I (R = H, Me) had pharmacol. activity equivalent to that of haloperidol but had lower toxicity and lower potency to induce catalepsy. Some aspects of structure-activity relationships are discussed.

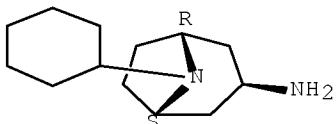
IT 76272-54-3

RL: RCT (Reactant); RACT (Reactant or reagent)  
(acylation of, with aminomethoxypyrimidinecarboxylic acid)

RN 76272-54-3 CAPLUS

CN 8-Azabicyclo[3.2.1]octan-3-amine, 8-cyclohexyl-, exo- (9CI) (CA INDEX NAME)

Relative stereochemistry.



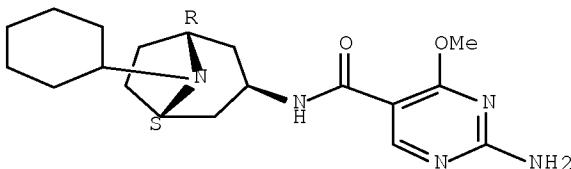
IT 91595-99-2P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn and antidopaminergic activity of)

RN 91595-99-2 CAPLUS

CN 5-Pyrimidinecarboxamide, 2-amino-N-(8-cyclohexyl-8-azabicyclo[3.2.1]oct-3-yl)-4-methoxy-, exo- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L3 ANSWER 13 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1981:65477 CAPLUS Full-text

DOCUMENT NUMBER: 94:65477

ORIGINAL REFERENCE NO.: 94:10669a,10672a

TITLE: Azabicycloalkyl derivatives and pharmaceutical compositions containing them

INVENTOR(S): Hadley, Michael Stewart; King, Francis David

PATENT ASSIGNEE(S): Beecham Group Ltd., UK

SOURCE: Eur. Pat. Appl., 63 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent

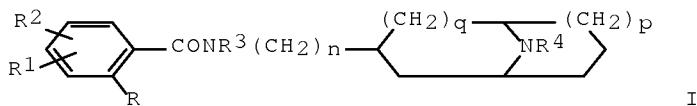
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 13138	A1	19800709	EP 1979-302978	19791220
EP 13138	B1	19831207		
R: AT, BE, CH, DE, FR, GB, IT, NL, SE				
EP 81054	A2	19830615	EP 1982-109116	19791220
EP 81054	A3	19830824		
EP 81054	B1	19861217		
R: AT, BE, CH, DE, FR, GB, IT, NL, SE				
AT 24320	T	19870115	AT 1982-109116	19791220
EP 220339	A1	19870506	EP 1985-115575	19791220
EP 220339	B1	19891108		
R: BE, CH, DE, FR, GB, IT, NL, SE				
DK 7905539	A	19800815	DK 1979-5539	19791221
JP 55092384	A	19800712	JP 1979-170199	19791226
US 4273778	A	19810616	US 1979-107413	19791226
AU 7954255	A	19800703	AU 1979-54255	19791228
AU 527837	B2	19830324		
ES 487379	A1	19801201	ES 1979-487379	19791228
ZA 7907054	A	19801231	ZA 1979-7054	19791228
CA 1218062	A1	19870217	CA 1979-342845	19791231
US 4336259	A	19820622	US 1980-200768	19801027
US 4544660	A	19851001	US 1981-271990	19810609
US 4599420	A	19860708	US 1983-469681	19830225
CA 1220473	A2	19870414	CA 1984-446870	19840206
US 4705858	A	19871110	US 1986-824458	19860131
JP 02072178	A	19900312	JP 1989-112779	19890501
JP 03075548	B	19911202		
PRIORITY APPLN. INFO.:				
		GB 1978-50380	A	19781230
		GB 1979-9262	A	19790315
		GB 1979-27831	A	19790809
		EP 1979-302978	A	19791220
		EP 1982-109116	A	19791220
		US 1979-107413	A3	19791226
		CA 1979-342845	A3	19791231
		US 1981-271990	A3	19810609
		US 1983-469681	A3	19830225

OTHER SOURCE(S): MARPAT 94:65477  
GI



AB Azabicycloalkanes I (R = alkoxy; R1, R2 = H, halogen, CF<sub>3</sub>, acyl, acylamino, NH<sub>2</sub>, optionally substituted CONH<sub>2</sub>, SO<sub>2</sub>NH<sub>2</sub>, alkylsulfonyl, NO<sub>2</sub>; R<sub>3</sub> = H, alkyl; R<sub>4</sub> = optionally substituted alkyl; n, p, q = 0-2) were prepared. Thus I [R = OMe, R<sub>1</sub> = 4-NHAc (II), R<sub>2</sub> = 5-Cl, R<sub>3</sub> = H, R<sub>4</sub> = CH<sub>2</sub>Ph, n = p = 0, q = 1] was obtained as a mixture of 3' $\alpha$ - and 3' $\beta$ -isomers by acylating 3-amino-8-benzylnortropane (III) and was deacylated to II (R<sub>1</sub> = 4-NH<sub>2</sub>). III was obtained by LiAlH<sub>4</sub> reduction of 8-benzyl-3-nortropanone oxime. II (R<sub>1</sub> = 4-NH<sub>2</sub>) inhibited apomorphine-induced stereotype behavior at  $\leq$ 10 mg/kg s.c. in rats and was antiemetic at 0.0025 mg/kg s.c. in dogs.

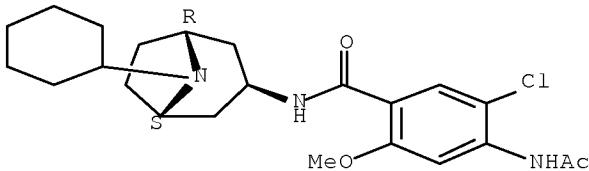
IT 76272-92-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation and deacetylation of)

RN 76272-92-9 CAPLUS

CN Benzamide, 4-(acetylamino)-5-chloro-N-(8-cyclohexyl-8-azabicyclo[3.2.1]oct-3-yl)-2-methoxy-, exo- (9CI) (CA INDEX NAME)

Relative stereochemistry.



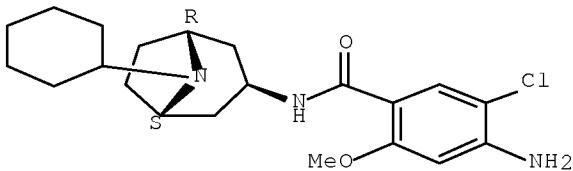
IT 76272-91-8P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation and dopamine antagonist and antiemetic activity of)

RN 76272-91-8 CAPLUS

CN Benzamide, 4-amino-5-chloro-N-(8-cyclohexyl-8-azabicyclo[3.2.1]oct-3-yl)-2-methoxy-, exo- (9CI) (CA INDEX NAME)

Relative stereochemistry.



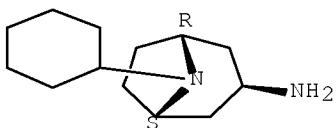
IT 76272-54-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation and reaction of, with methoxybenzoyl chloride derivative)

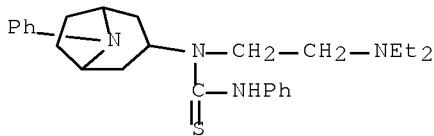
RN 76272-54-3 CAPLUS

CN 8-Azabicyclo[3.2.1]octan-3-amine, 8-cyclohexyl-, exo- (9CI) (CA INDEX NAME)

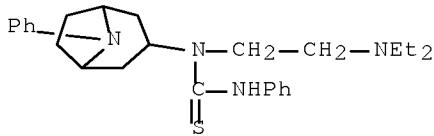
Relative stereochemistry.



L3 ANSWER 14 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 1961:82268 CAPLUS Full-text  
 DOCUMENT NUMBER: 55:82268  
 ORIGINAL REFERENCE NO.: 55:15609d-e  
 TITLE: State of transforming deoxyribonucleic acid (DNA)  
       during the first phase of bacterial transformation  
 AUTHOR(S): Taylor, Harriett Ephrussi  
 CORPORATE SOURCE: Lab. genetique physiol., Gif-sur-Yvette, Fr.  
 SOURCE: Comptes Rendus des Seances de la Societe de Biologie  
       et de Ses Filiales (1960), 154, 1951-5  
 CODEN: CRSBAW; ISSN: 0037-9026  
 DOCUMENT TYPE: Journal  
 LANGUAGE: Unavailable  
 AB Expts. with pneumococci seemed to indicate that at the stage of fixation of added transforming DNA the latter is firmly bound to a protein of the receptor cell, and that it retains its high mol. weight until liberation within the cell by growth processes.  
 IT 123935-68-2P, Urea, 1-(2-diethylaminoethyl)-3-phenyl-1-(8-phenyl-3-nortropanyl)-2-thio-  
     RL: PREP (Preparation)  
         (preparation of)  
 RN 123935-68-2 CAPLUS  
 CN Urea, 1-(2-diethylaminoethyl)-3-phenyl-1-(8-phenyl-3-nortropanyl)-2-thio-  
     (6CI) (CA INDEX NAME)



L3 ANSWER 15 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 1961:82267 CAPLUS Full-text  
 DOCUMENT NUMBER: 55:82267  
 ORIGINAL REFERENCE NO.: 55:15609c-d  
 TITLE: Action of lysozyme on Haemophilus pertussis  
 AUTHOR(S): Dumazert, C.; Ghiglione, C.  
 SOURCE: Bulletin de la Societe de Pharmacie de Marseille  
       (1960), 9, 145-59, 161-71  
 CODEN: BSPMAC; ISSN: 0560-5237  
 DOCUMENT TYPE: Journal  
 LANGUAGE: Unavailable  
 AB Action of lysozyme on bacterial suspensions of H. pertussis resulted in the isolation of a glucoside fraction and a protein fraction. The glucoside contains glucose, galactose, and an unidentified N base. The protein has not been fully characterized. Immunological studies on the glucoside fraction indicate properties similar to a hapten isolated from Pneumococcus.  
 IT 123935-68-2P, Urea, 1-(2-diethylaminoethyl)-3-phenyl-1-(8-phenyl-3-nortropanyl)-2-thio-  
     RL: PREP (Preparation)  
         (preparation of)  
 RN 123935-68-2 CAPLUS  
 CN Urea, 1-(2-diethylaminoethyl)-3-phenyl-1-(8-phenyl-3-nortropanyl)-2-thio-  
     (6CI) (CA INDEX NAME)



L3 ANSWER 16 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN

ACCESSION NUMBER: 1959:2191 CAPLUS

DOCUMENT NUMBER: 53:2191

ORIGINAL REFERENCE NO.: 53:430h-i, 431a-i, 432a-i

TITLE: Tertiary amino substituted 1,5-iminocycloalkanes

INVENTOR(S): Archer, Sydney

PATENT ASSIGNEE(S): Sterling Drug Inc.

DOCUMENT TYPE: Patent

LANGUAGE: Unavailable

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2845427		19580729	US 1955-483808	19550124

AB N-Substituted 1,5-iminocycloalkanes (I) attached at the 3-position through an O, S, or N atom to a tertiary amino alkyl group, which are useful for the reduction of hypertension (the salts and quaternary derivs. are even more active), are prepared by treating a 3-oxo derivative of I with a tertiary amino alkylamine and reducing the resulting imine by condensing the 3-alkali metal sulfide or oxide derivative of I with a tertiary amino alkyl halide and (or) by condensing 3-halo derivative of I with the alkali metal salt of a tertiary amino alkyl mercaptan or hydroxide. 3-Tropolone (30 g.), 24 g. Et<sub>2</sub>N(CH<sub>2</sub>)<sub>2</sub>NH<sub>2</sub>, 1.2 g. PtO<sub>2</sub>, and 50 ml. EtOH was shaken 1 hr. under 50 lb. H<sub>2</sub> filtered, and the filtrate distilled to give 33.2 g. 3-(2-diethylaminoethylamino)-tropane (II), b0.5 111-15°; tri-HCl salt, m. 267-71°; picrate, m. 163.5-6°; dimethiodide, m. 269°; dimethobromide, m. 289-90°. II (59 g.) was cooled to solid CO<sub>2</sub> temperature, 54 ml. 100% HCO<sub>2</sub>H and 24.6 ml. 36% H<sub>2</sub>CO added, the mixture heated on the steam bath 16 hrs., cooled and made basic, extracted with Et<sub>2</sub>O, and the product distilled to yield 42.5 g. 3-[(2-diethylaminoethyl)methylamino]tropane, b0.8-1 120-3°, n<sub>25D</sub> 1.4871; tri-HBr salt, m. above 140°; dimethiodide, m. 242-4°; dimethobromide, m. 245-7°; diethiodide, m. 237-8°. Similarly the following 3-substituted derivs. of tropane were prepared (side chain, b.p./mm., and salts with their m.p. given): Me<sub>2</sub>N(CH<sub>2</sub>)<sub>2</sub>NH, 101.5-3°/0.5 (n<sub>25D</sub> 1.4880); Me<sub>2</sub>N(CH<sub>2</sub>)<sub>2</sub>NMe, 104-7°/1.2 (n<sub>25D</sub> 1.4900-9), di-MeI 238-41°; C<sub>5</sub>H<sub>10</sub>N(CH<sub>2</sub>)<sub>3</sub>NH, 141-50°/0.5; C<sub>5</sub>H<sub>10</sub>N(CH<sub>2</sub>)<sub>3</sub>NMe, 141-8°/0.2 (n<sub>25D</sub> 1.5057), di-MeI 222-3°, tri-MeI 207-14°; C<sub>5</sub>H<sub>10</sub>N(CH<sub>2</sub>)<sub>2</sub>NH, 132-3°/0.5, tri-HCl 275-7°, di-MeI 293°; C<sub>5</sub>H<sub>10</sub>N(CH<sub>2</sub>)<sub>2</sub>NMe, 118.5-26°/0.07, tri-HBr 220-4.5°, di-MeI 259-66°, di-EtI 215-19°; C<sub>4</sub>H<sub>4</sub>N(CH<sub>2</sub>)<sub>3</sub>NH, 140-4°/0.05; C<sub>4</sub>H<sub>4</sub>N(CH<sub>2</sub>)<sub>3</sub>NMe, 129-31°/0.2 (n<sub>25D</sub> 1.5031-40), di-MeI 226-8°; C<sub>4</sub>H<sub>4</sub>N(CH<sub>2</sub>)<sub>2</sub>NH, 130-5°/0.5, di-MeI 290-3°; C<sub>4</sub>H<sub>4</sub>N(CH<sub>2</sub>)<sub>2</sub>NMe, 122-4°/0.3 (n<sub>25D</sub> 1.5055-60), di-MeI 205-20°; C<sub>4</sub>H<sub>4</sub>N(CH<sub>2</sub>)<sub>4</sub>NH, 142-8°/0.3 (n<sub>25D</sub> 1.5038-41); C<sub>4</sub>H<sub>4</sub>N(CH<sub>2</sub>)<sub>4</sub>NMe, 138-41°/0.2 (n<sub>25D</sub> 1.5029); OC<sub>4</sub>H<sub>8</sub>N(CH<sub>2</sub>)<sub>2</sub>NH, 133-5°/0.4 (n<sub>25D</sub> 1.5066), tri-HCl 245-9.5°, di-MeI 264-5°; OC<sub>4</sub>H<sub>8</sub>N(CH<sub>2</sub>)<sub>2</sub>NMe, 124-30°/0.1 (n<sub>25D</sub> 1.5079-83), tri-HBr 252-4°, di-MeI 218-20°; Me<sub>2</sub>N(CH<sub>2</sub>)<sub>3</sub>NH, 112-14°/1.7 (n<sub>25D</sub> 1.4990), picrate 230°; Me<sub>2</sub>N(CH<sub>2</sub>)<sub>3</sub>NMe, 106-12°/0.5 (n<sub>25D</sub> 1.4885-8), picrate 231°; Et<sub>2</sub>N(CH<sub>2</sub>)<sub>3</sub>NH, 120-5°/0.1 (n<sub>25D</sub> 1.4862); Et<sub>2</sub>N(CH<sub>2</sub>)<sub>3</sub>NMe, 120-30/0.1 (n<sub>25D</sub> 1.4870), di-MeI 222-7°; PhMeN(CH<sub>2</sub>)<sub>2</sub>NH (III), 167-73°/0.1; PhEtN(CH<sub>2</sub>)<sub>2</sub>NH (IV), 174-7°/0.6, MeI 226-8°; p-MeC<sub>6</sub>H<sub>4</sub>NMe(CH<sub>2</sub>)<sub>2</sub>NH, 164-73°/0.3 (n<sub>25D</sub> 1.5532); p-MeOC<sub>6</sub>H<sub>4</sub>NMe(CH<sub>2</sub>)<sub>2</sub>NH, 179-

83°/0.5 (n24D 1.5560); NH(CH<sub>2</sub>)<sub>2</sub>NH (bis compound), 178-81°/0.6; and NMe(CH<sub>2</sub>)<sub>2</sub>NMe (bis compound), 192-200°/1.5, di-MeI 273-4°. II (3.8 g.) and 2.2 g. PhNCS heated in MeOH gave 3.7 g. 1-(2-diethylaminoethyl)-1-(3-tropanyl)-3-phenylthiourea (V), m. 170.5-2°. The following derivs. of II were prepared (group replacing the H of the secondary amine, b.p./mm., or m.p., and certain salts with their m.p. given): MeCH:CHNHCS, 97-100°; EtNHCS, 122-4°; 4-EtOC<sub>6</sub>H<sub>4</sub>NHCS, 160-1°; Ac (VI), 142-4°/0.09 (n25D 1.4980), picrate 198-200°; EtCO (VII), 160°/0.5 (n25D 1.4940-5), picrate 173-6°; and PrCO (VIII), 162-6°/0.7 (n28D 1.4935), picrate 194-6°. VI, VII, and VIII were reduced with LiAlH<sub>4</sub> in Et<sub>2</sub>O to the following N-substituted derivs. of II (substituent, b.p./mm., n28D, and salts given): Et, 142°/2, 1.4845, di-MeI 230-1°, di-EtI 226°; Pr, 119-26°/0.1, 1.4835, picrate 223°, di-MeI 203-9°; and Bu, 125-30°/0.1, 1.4839, picrate 208-10°. Other 3-substituted tropane derivs. that were prepared are (side chain, b.p. m/m., and salts given): C<sub>4</sub>H<sub>4</sub>N(CH<sub>2</sub>)<sub>2</sub>N(CHO), 166-72°/0.9 (n24D 1.5131); PhEtN(CH<sub>2</sub>)<sub>2</sub>N(CHO), 200-7°/0.1-0.2; PhEtN(CH<sub>2</sub>)<sub>2</sub>NMe, 182-7°/15 (n24D 1.5518), di MeI 240-2°; p-MeC<sub>6</sub>H<sub>4</sub>NMe(CH<sub>2</sub>)<sub>2</sub>N(CHO), 95-7°; p-MeC<sub>6</sub>H<sub>4</sub>NMe(CH<sub>2</sub>)<sub>2</sub>NMe, 174-6°/0.5 (n24D 1.5508-10), HCl 168°, tri-MeI 215°; p-MeOC<sub>6</sub>H<sub>4</sub>NMe(CH<sub>2</sub>)<sub>2</sub>N(CHO), 112-14°; p-MeOC<sub>6</sub>H<sub>4</sub>NMe(CH<sub>2</sub>)<sub>2</sub>NMe (IX), 162-6°/0.1 (n25D 1.5518), picrate 205-7°, di-MeI 195-8°. Formic acid (26.5 ml.), 500 ml. H<sub>2</sub>O, and 29 g. III followed by 10 ml. 37% H<sub>2</sub>CO was heated 15 hrs. on the steam bath to give 1-methyl-4-(3-tropanyl)-1,2,4,5-tetrahydro-1,4-benzodiazepine (X), b0.6 155-65°; di-MeI salt (XI), m. 264-7°; di-EtI salt, m. 208-10°. X was methylated in the 7-position with H<sub>2</sub>CO and HCO<sub>2</sub>H, b0.2 163°; picrate, m. 230-1°; methiodide, m. 274-6°. XI subjected to a Hofmann degradation gave 1-[(2-dimethylaminobenzyl)vinylamino]-3-dimethylamino-5-cycloheptene; dipicrate, m. 193-4°. IV, H<sub>2</sub>CO, and HCO<sub>2</sub>H gave the 1-Et homolog of X, b0.5 174-8° (di-MeI salt, m. 269-71°; MeI salt, m. 235-8°; di-MeBr salt, m. 262-2.5°; di-EtBr salt, m. 253-4°), and IX under these conditions gave the 7-methoxy derivative of X, b0.1 180-5°; picrate, m. 239-40°. III heated with 98% HCO<sub>2</sub>H gave 3-[2-(phenylmethylaminoethyl)formylamino]tropane, b0.5 216-22°, which was reduced with LiAlH<sub>4</sub> to the N-Me derivative, b0.6 160-5°; dimethiodide, m. 255°; dimethobromide, m. 258°. Tropine (60 g.) in 50 ml. MePh was added to 9.2 g. Na in 100 ml. MePh, the mixture refluxed 4 hrs. and 42.8 g. Me<sub>2</sub>N(CH<sub>2</sub>)<sub>2</sub>Cl added, the mixture refluxed 3 hrs., aqueous MeOH added, and distilled to give 17.3 g. 3-(2-dimethylaminoethoxy)tropane, b0.9 85-5.5°, n25D 1.4836; diperchlorate, m. 243-6°; dimethiodide, m. 314-15°; diethiodide, m. 269-75°. Similarly, the following 3-substituted tropanes were prepared (side chain, b.p./mm., and salts and their m.p. given): Et<sub>2</sub>N(CH<sub>2</sub>)<sub>2</sub>O, 101°/0.07 (n25D 1.4758), di-MeI 301-2°; C<sub>5</sub>H<sub>10</sub>N(CH<sub>2</sub>)<sub>2</sub>O, 106-9°/0.07, di-MeI 305°; C<sub>5</sub>H<sub>10</sub>N(CH<sub>2</sub>)<sub>3</sub>O, 115°/0.1, di-MeI above 305°; C<sub>4</sub>H<sub>4</sub>N(CH<sub>2</sub>)<sub>2</sub>O, 134°/2.8 (n25D 1.4932), di-MeI 313-14°; Et<sub>2</sub>N(CH<sub>2</sub>)<sub>3</sub>O(CH<sub>2</sub>)<sub>3</sub>O, 94-6°/0.2, di-MeI 300°. Pseudotropine, Na, and Et<sub>2</sub>(CH<sub>2</sub>)<sub>2</sub>Cl in C<sub>6</sub>H<sub>6</sub> gave 3-(2-diethylaminoethoxy)pseudotropane, b0.25, 109-12°, n25D 1.4775; dimethiodide, m. 307-8°. Tropanone (69.5 g.), 63.8 g. Et<sub>2</sub>N(CH<sub>2</sub>)<sub>2</sub>NH<sub>2</sub>, and 500 mg. ZnCl<sub>2</sub> in MePh was heated 64 hrs. using an H<sub>2</sub>O separator to yield 92.2 g. 3-(2-diethylaminoethylimino)tropane (XII), b0.6 117-31°. XII was reduced by Na and EtOH to a mixture of 3-(2-diethylaminoethylamino)tropane and pseudotropane. The mixture of isomers and PhNCS gave V and the isomeric pseudotropane, m. 138-9.5°. By this procedure pseudopelletierine (XIII) and C<sub>5</sub>H<sub>10</sub>N(CH<sub>2</sub>)<sub>2</sub>NH<sub>2</sub> yielded 3-[2-(1-piperidyl)ethylimino]-9-methylgranatanine, b1 164-76°, n25D 1.5235, which was reduced by Na in Me<sub>2</sub>CH(CH<sub>2</sub>)<sub>3</sub>OH to a mixture of isomers of the corresponding amine which was treated with PhNCS in MeOH to yield a mixture of isomers of the thiourea (XIV), m. 174.5-6°, (XV) m. 173-4.5° (AcOEt). XIV (7.3 g.), MeOH, and 25 ml. 4N HCl in EtOH was evaporated, the residue heated 30 min. at 100°, dissolved in EtOH, and the solution cooled to yield 3-[2-(1-piperidyl)ethylamino]-9-methylgranatanine; tri-HCl salt (XVI), m. 285-7°. XV treated in this manner gave an isomer of XVI, m. 276°. Similarly, XIII with the appropriate amine gave the following 3-substituted derivs. of 9-methylgranatanine (side chain, b.p./mm., and salts with their m.p. given; when isomers were obtained, both m.p.'s given): C<sub>4</sub>H<sub>4</sub>N(CH<sub>2</sub>)<sub>2</sub>NH,

144-6°/1 (n24D 1.5252); C4H4N(CH2)2NH, 155-7°/2 (n25D 1.5102), di-MeI 278°; C4H4N(CH2)2(PhNHCS)N, 173-4°; Et2N(CH2)2NH, 131-9°/0.7 (n25D 1.5050); Et2N(CH2)2NH, 128-30°/0.6 (n25D 1.4920), tri-HCl 278° and 185°, di-MeI 277-9°; Et2N(CH2)2(PhNHCS)N, 189-91° and 135-6°. Concentrated HCl (0.13 ml.) was added to 160 g. 2,5-diethoxytetrahydrofuran in 150 ml. H2O, the suspension stirred 2 hrs. at 48-50° and cooled, 202 g. (EtO2CCH2)2CO, 100 ml. H2O, 107 g. PhCH2NH2, and 83 ml. HCl added, the mixture stirred overnight, 250 ml. HCl added, heated while 270 ml. H2O was distilled, the residue filtered, the filtrate made basic with NaOH, 500 g. K2CO3 added, and the mixture extracted with Et2O to yield 102 g. 8-benzyltropanone (XVII), b0.4 134-7°, n25D 1.5526. XVII yielded 3-(2-diethylaminoethylamino)-8-benzylnortropane, b0.25 161-8°, n25D 1.5235; tri-HCl salt, m. 264-6°; dimethiodide, m. 255-7°; phenylthiourea derivative, m. 138-9°. The following 8-benzylnortropane derivs. are described (side chain and phenyl substituents, b.p./mm. or m.p., and salts given): 4'-MeO, 3-oxo, 179-84°/0.1 (n25D 1.5538), HCl 203-4°; 4'-MeO, 3-Et2N(CH2)2HN, tri-HCl 277-8°, di-MeI 229-30°; 2',3'-di-MeO, 3-oxo, 178-99°/0.5, HCl 201-2°; 2'-3'-di-MeO, 3-Et2N(CH2)2HN, tri-HCl 234-7°, di-MeI 226-8°; 3,'4'-OCH2O, 3-oxo, tri-HCl 223-3.5°; 3',4'-OCH2O, 3-Et2N(CH2)2HN, tri-HCl 275-6°, di-MeI 234-7°; 3',4'-OCH2O, 3-Et2N(CH2)2(PhNHCS)N, 148-9°; 4'-Cl, 3-oxo, 168-80°/0.8; 4'-Cl, 3-Et2N(CH2)2HN, di-MeI 232-4°, di-MeBr 228-30.5°; 2'-Cl, 3-Et2N(CH2)2(PhNHCS)N, 124-6°; 2'-Cl, 3-C4H4N(CH2)2HN, tri-HCl 253°, di-MeI 218-20°; 2'-MeO, 3-oxo, 174-81°/0.2-0.5 (n25D 1.5061-5), HCl 177-8°; 2'-MeO, 3-Et2N(CH2)2HN, tri-HCl 248-51°, di-MeI 218.5-21.5°; 2',4'-di-Cl, 3-oxo, 185-7°/1.5, tri-HCl 216°; and 2,4-di-Cl, 3-Et2N(CH2)2NH, di-MeI 237-9°. 8-Phenylnortropane, m. 107-9°, was prepared by the method used for XIII and reaction with Et2N(CH2)2NH2, PtO2, and H gave 3-(2-diethylaminoethylamino)-8-phenylnortropane (XVIII), b0.2 153-68°, which with PhNCS gave the thiourea derivative, m. 161-3°, and with Ac2O yielded N-Ac derivative of XVIII, b0.2 183-98°, n25D 1.5470, which was reduced to the N-Et derivative of XVIII, b0.9 180-4°, n30D 1.5370. PhEtN(CH2)2NH2 (35 g.), 32 g. XIII, 1 g. ZnCl2, and 200 ml. MePh gave 3-(2-phenylmethylaminoethylamino)-9-methylgranatanine, b0.2-0.9 160-84°, n30D 1.5575, from which the following N-substituted derivs. were prepared (b.p./mm. and salts with their m.p. given): HCO, 190-220°/0.7; Me, 161-6°/0.15, picrate 191-4°, di-MeI 225-7°; Ac, 200-14°/0.2; and Et, 162-7°/0.1, picrate 203-5°.

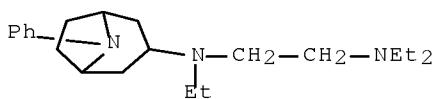
IT 102457-13-6P, Nortropane, 3-[(2-diethylaminoethyl)ethylamino]-8-phenyl- 102463-23-0P, Nortropane, 3-[(2-diethylaminoethyl)methylamino]-8-phenyl- 102709-02-4P, Nortropane, 3-[(2-diethylaminoethyl)amino]-8-phenyl- 110147-72-3P, Nortropane, 3-[N-(2-diethylaminoethyl)acetamido]-8-phenyl- 123935-68-2P, Urea, 1-(2-diethylaminoethyl)-3-phenyl-1-(8-phenyl-3-nortropanyl)-2-thio-

RL: PREP (Preparation)

(preparation of)

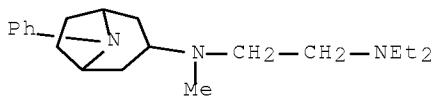
RN 102457-13-6 CAPLUS

CN Nortropane, 3-[(2-diethylaminoethyl)ethylamino]-8-phenyl- (6CI) (CA INDEX NAME)

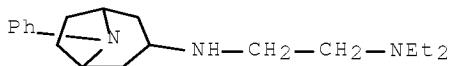


RN 102463-23-0 CAPLUS

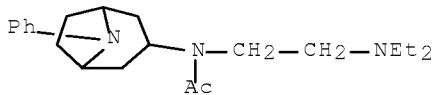
CN Nortropane, 3-[(2-diethylaminoethyl)methylamino]-8-phenyl- (6CI) (CA INDEX NAME)



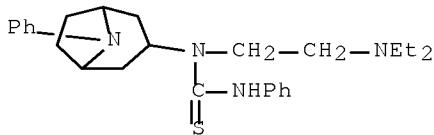
RN 102709-02-4 CAPLUS  
 CN Nortropane, 3-[(2-diethylaminoethyl)amino]-8-phenyl- (6CI) (CA INDEX NAME)



RN 110147-72-3 CAPLUS  
 CN Nortropane, 3-[N-(2-diethylaminoethyl)acetamido]-8-phenyl- (6CI) (CA INDEX NAME)



RN 123935-68-2 CAPLUS  
 CN Urea, 1-(2-diethylaminoethyl)-3-phenyl-1-(8-phenyl-3-nortropanyl)-2-thio- (6CI) (CA INDEX NAME)



L3 ANSWER 17 OF 19 CAPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 1958:6906 CAPLUS  
 DOCUMENT NUMBER: 52:6906  
 ORIGINAL REFERENCE NO.: 52:1292a-i,1293a-b  
 TITLE: 3-(Monocarbocyclic aryl-lower alkyl)amino-1,5-iminocycloalkanes  
 INVENTOR(S): Archer, Sydney  
 PATENT ASSIGNEE(S): Sterling Drug Inc.  
 DOCUMENT TYPE: Patent

LANGUAGE: Unavailable

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2798874		19570709	US 1955-502745	19550420

GI For diagram(s), see printed CA Issue.

AB Compds. of the general formula RN.CH.CH<sub>2</sub>.(CH<sub>2</sub>)<sub>m</sub>.CH.CH<sub>2</sub>.CH(NR'CnH<sub>2n</sub>Ar).CH<sub>2</sub> and their salts, where R is lower alkyl, monocarbocyclic aryl, or aryl lower alkyl, R' is H or lower alkyl, m is 1-2, n is 1-6, and Ar is a monocarbocyclic aryl group, are useful in reducing hypertension and exhibit ganglionic blocking action in cats and dogs. They are prepared by reaction of a 3-tropinone (via the Robinson synthesis) and ArCnH<sub>2n</sub>NH<sub>2</sub> under hydrogenation conditions. E.g., 45 g. 3-tropinone (I), 32 g. PhCH<sub>2</sub>NH<sub>2</sub>, 1.0 g. PtO<sub>2</sub>, and 150 ml. EtOH are shaken 4 hrs. at 55° with H at 50 lb. per sq. in. One mole H is taken up. After filtration, the mixture is distilled and redistd. to obtain 34.8 g. 3-benzylaminotropane (II), b0.8 140-2°, n<sub>25</sub>D 1.5450; picrate, m. 160-1°. II (29.6 g.) is cooled to 20° and 28.2 cc. 98% HCO<sub>2</sub>H added portionwise followed by 13 cc. 36% HCHO solution, the mixture warmed to room temperature, heated 17 hrs. on a steam bath, poured into ice H<sub>2</sub>O, made basic with 35% NaOH solution, extracted with ether, dried over K<sub>2</sub>CO<sub>3</sub>, and distilled to get 21.2 g. 3-(benzylmethylamino)tropane (III), b0.3 135-8°, n<sub>25</sub>D 1.5416; picrate, m. 230-2° (from HCONMe<sub>2</sub>); methiodide, m. 233.0-7.5° (decomposition). I (42 g.), 52.5 cc. 5.82N MeNH<sub>2</sub> in MeOH, 1.5 g. PtO<sub>2</sub>, and 100 ml. MeOH treated similarly yield 38.3 g. 3-methylaminotropane (IV), b<sub>23</sub> 109-10°, n<sub>25</sub>D 1.4934. When 15.2 g. IV, 12.6 g. PhCH<sub>2</sub>Cl, and 13.8 g. K<sub>2</sub>CO<sub>3</sub> in 100 cc. PhMe are heated 4 hrs. under reflux and 10% K<sub>2</sub>CO<sub>3</sub> solution then added, three layers are formed. The bottom (aqueous) layer is discarded; the top (PhMe) layer is distilled to dryness, the residue dissolved in ether, filtered, and the filtrate distilled to get 5.6 g. III, b0.8 130-6°. The middle layer is taken up in CHCl<sub>3</sub>, washed with H<sub>2</sub>O, and the CHCl<sub>3</sub> distilled, ether added to an EtOH solution of the residue, and the solid (3.7 g.) separated and recrystd. from EtOH-ether to obtain the 8-benzochloride of III (V), m. 224.0-5.5° (decomposition); 8-(4-nitrobenzobromide) (VI), m. 220-3° (decomposition); 8-(4-chlorobenzochloride) (VII), m. 226-8° (decomposition); 8-(3,4-dichlorobenzochloride) (VIII), m. 232-5° (decomposition); 8-(p-methoxybenzochloride); 8-(p-methylbenzochloride). 3-(4-Chlorobenzylamino)tropane (IX), b0.2 135-53°; picrate, m. 185-7°. 3-(2-Phenylethylamino)-, 3-(3-phenylpropylamino)-, and 3-(2-phenylpropylamino)tropane are prepared by analogous methods. IX is heated with 1 molar equivalent PhNCS to obtain the phenylthiureide, m. 130-2°. Replacement of I in the synthesis of IX with pseudopelletierine gives 3-(4-chlorobenzylamino)-9-methylgranatanine. IX (18.0 g.), 15 ml. 98% HCO<sub>2</sub>H, and 6.85 ml. 37% HCHO solution yield 12.4 g. 3-[(4-chlorobenzyl)methylamino]tropane (X), b0.3 140°; 8-methiodide (XI), m. 255-6° (decomposition); 8-methobromide, m. 261-3° (decomposition); 8-(4-nitrobenzobromide), m. 210-12° (decomposition). X, b0.1-0.2 144-6°, n<sub>25</sub>D 1.5483, and its 8-(4-chlorobenzochloride) (XII), m. 202.5-205° (decomposition), are prepared by the method used for III and V. The 8-(3,4-dichlorobenzochloride) of XII, m. 200-3° (decomposition); 8-(2-hydroxyethobromide), m. 219-21°. A mixture of 50 g. 4-Et<sub>2</sub>NC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>NH<sub>2</sub> and 200 ml. 12% NH<sub>3</sub> in MeOH is hydrogenated (Raney Ni) 3 hrs. at 21-2° at an initial pressure of 890 lbs. per sq. in., filtered, distilled, and redistd. to obtain 23.2 g. 4-diethylaminobenzylamine (XIII), b0.1 122-8°, n<sub>25</sub>D 1.5592. Hydrogenation of 19.0 g. I, 23.2 g. XIII, and 1 g. PtO<sub>2</sub> in 200 ml. absolute EtOH as before, solution of the crude product in absolute EtOH, and addition of excess alc. HCl give 21.5 g. 3-(4-diethylaminobenzylamino)tropane trihydrochloride dihydrate, m. 195° (decomposition); picrate of free base, m. 185° (decomposition). The phenylthiureide m. 145-7°; 8-methiodide (XIV), m. 240-5° (decomposition); 8-(4-chlorobenzochloride) (XV), m. 208-11°

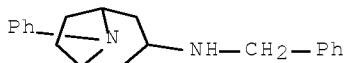
(decomposition); 8-(3,4-dichlorobenzochloride), m. 200-3° (decomposition); 8-(4-nitrobenzobromide), m. 189-91°. 3-(Benzylacetylaminotropane is prepared by treating II with Ac<sub>2</sub>O followed by hydrolysis; reduction with LiAlH<sub>4</sub> yields 3(benzylethylamino)tropane. A solution of 36.2 g. 2,5-diethoxytetrahydrofuran in 240 cc. H<sub>2</sub>O containing 0.6 ml. concentrated H<sub>2</sub>SO<sub>4</sub> is warmed 15 min. on a steam bath, cooled, and added to a solution of 97 g. CO(CH<sub>2</sub>CO<sub>2</sub>H)<sub>2</sub>, 146 NaOAc·3H<sub>2</sub>O, and 27 PhNH<sub>2</sub> in 3.5 l. H<sub>2</sub>O. After standing overnight, the solid is collected, dissolved in one 1.5% aqueous HCl at 60°, cooled, made alkaline with NH<sub>3</sub>, and the product recrystd. from dilute MeOH to obtain 11.4 g. 8-phenylnortropane (XVI), m. 107-9°; hydrogenation of a mixture of XVI, PhCH<sub>2</sub>NH<sub>2</sub>, and PtO<sub>2</sub> in EtOH gives 3-benzylamino-8-phenylnortropane. V, VI, VII, VIII, XI, and XII are 60, 54, 74, 128, 30, and 100% as effective, resp., as hexamethylenebis(trimethylammonium bromide) in blockade of the sympathetic ganglia when measured by the carotid occlusion test in dogs. X, XIV, and XV are similarly 35, 26, and 210% as effective, resp., in cats.

IT 102552-20-5P, Nortropane, 3-benzylamino-8-phenyl-

RL: PREP (Preparation)  
(preparation of)

RN 102552-20-5 CAPLUS

CN Nortropane, 3-benzylamino-8-phenyl- (6CI) (CA INDEX NAME)



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ACCESSION NUMBER: 1957:86038 CAPLUS

DOCUMENT NUMBER: 51:86038

ORIGINAL REFERENCE NO.: 51:15607c-i,15608a-i,15609a-h

TITLE: Tertiary amino-substituted compounds of the tropane and granatanine series

PATENT ASSIGNEE(S): Sterling Drug Inc.

DOCUMENT TYPE: Patent

LANGUAGE: Unavailable

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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GB 762256		19561128	GB	

AB Tertiary amino substituted tropanes, granatanines, and their salts are prepared 3-Tropanone (30 g.), 24 g. 2-diethylaminoethylamine, 1.2 g. PtO<sub>2</sub>, and 50 ml. EtOH is shaken in 50 lb./sq. in. H 2.5 hrs., the product filtered, the filtrate concentrated, and distilled to give 33.2 g. 3-(2-diethylaminoethylamino)tropane, b5 111-15°; picrate, m. 163.5-6° (from aqueous EtOH); trihydrochloride monohydrate, m. 267-71° (from 95% EtOH, MeOH); bismethiodide, m. 269° (from dilute MeOH) (decomposition). To 59 g. 3-[(2-diethylaminoethyl)amino]tropane cooled to -40° is added 54 ml. 100% HCO<sub>2</sub>H followed by 24.6 ml. 36% HCHO, the mixture heated to 100° 16 hrs., treated with 35% NaOH, extracted with Et<sub>2</sub>O, and then distilled to yield 42.5 g. 3-[(2-diethylaminoethyl)methylamino]tropane, b-1.0 120-3°, nD<sub>25</sub> 1.4871. Similarly the following compds. are prepared: 3-[(2-diethylaminoethyl)amino]tropane bismethobromide, m. 289-90° (from MeOH) (decomposition); 3-[(2-diethylaminoethyl)methylamino]tropane trihydrobromide, m. 140° (from MeOH); 3-[(2-dimethylaminoethyl)amino]tropane, b0.5 101.5-3°, nD<sub>25</sub> 1.4880; 3-[(2-

dimethylaminoethyl)methylamino]tropane, b1.2 104-7°, nD25 1.4900-9, m. 238-41° (decomposition); 3-[3-(1-piperidyl)propylamino]tropane, b0.2 141.8-°, nD25 1.5057; 3-[3-(1-piperidyl)propyl]methylamino]tropane bisethiodide, m. 222-33°; 3-[3-(1-piperidyl)propyl]methylamino]tropane trismethiodide, m. 207-14°; 3-[2-(1-piperidyl)ethylamino]tropane, b0.5 132-3°; 3-[2-(1-piperidyl)ethylamino]tropane trihydrochloride, m. 275-7°; 3-[2-(1-piperidyl)ethyl]methylamino]tropane bis-methiodide, m. 293°; 3-[2-(1-piperidyl)ethyl]methylamino]tropane trihydrobromide, m. 220-4.5°; 3-[2-(1-piperidyl)ethyl]methylamino]tropane bismethiodide, m. 259-60°; 3-[2-(1-piperidyl)ethyl]methylamino]tropane bisethiodide, m. 215-19°; 3-[3-(1-pyrrolidyl)propylamino]tropane, b0.05 140-4°; 3-[3-(1-pyrrolidyl)propyl]methylamino]tropane, b0.2 129-31°, nD25 1.5031-40; 3-[3-(1-pyrrolidyl)propyl]methylamino]tropane bismethiodide, m. 226-8°; 3-[2-(1-pyrrolidyl)ethylamino]tropane, b0.5 130-5°; 3-[2-(1-pyrrolidyl)ethylamino]tropane bismethiodide, m. 290-3° (decomposition); 3-[2-(1-pyrrolidyl)ethyl]methylamino]tropane, b0.3 122-4°, nD25 1.5055-60; 3-[2-(1-pyrrolidyl)ethyl]methylamino]tropane bismethiodide, m. 205-20°; 3-[4-(1-pyrrolidyl)butylamino]tropane, b0.3 142-8°, nD25 1.5038-41; 3-[4-(1-pyrrolidyl)butyl]methylamino]tropane, b0.2 138-40°, nD25.5 1.5029; 3-[2-(4-morpholinylethylamino]tropane, b0.4 133-5°, nD25 1.5066; 3-[2-(4-morpholinylethylamino]tropane trihydrochloride, m. 245-9° (with decomposition); 3-[2-(4-morpholinyl)ethylamino]tropane bismethiodide, m. 264.5-5° (decomposition); 3-[2-(4-morpholinyl)ethyl]methylamino]tropane, b0.1 124-30°, nD25 1.5079-83; 3-[2-(4-morpholinyl)ethyl]methylamino]tropane trihydrobromide, m. 252-4° (decomposition); 3-[2-(4-morpholinyl)ethyl]methylamino]tropane bismethiodide, m. 218-20°; 3-(3-dimethylaminopropylamino)tropane, b1.7 112-14°, nD24 1.4990 (tripicrate, m. 230°); 3-[3-dimethylaminopropyl]methylamino]tropane, b0.5 106-12°, nD26 1.4885-8 [picrate, m. 231° (decomposition)]; 3-(3-diethylaminopropylamino)tropane, b0.1 120-5°, nD25 1.4862 [picrate, m. 212° (decomposition)]; 3-[3-diethylaminopropyl]methylamino]tropane, b0.1 120-3°, nD25 1.4870; 3-[3-diethylaminopropyl]methylamino]tropane bismethiodide, m. 222-7°. Tropine (60 g.), 150 ml. PhMe, and 9.2 g. Na is refluxed 4 hrs., then 3 more hrs. with 42.8 g. 2-dimethylaminoethyl chloride in 50 ml. PhMe, aqueous MeOH added to the cooled product, and the organic layer separated, concentrated, and distilled to yield 17.3 g. 3-(2-diethylaminoethoxy)tropane, b0.9 85-0.5°, nD25 1.4836; bisperchlorate, m. 243-6° (from aqueous AcOH); bismethiodide, m. 314-5° (from MeOH) (decomposition). Similarly, the following compds. are prepared: 3-(2-diethylaminoethoxy)tropane, b0.07 101°, nD25 1.4758; 3-(2-diethylaminoethoxy)tropane bismethiodide, m. 301-2° (decomposition); 3-[2-(1-piperidyl)ethoxy]tropane, b0.07 106-9°; 3-[2-(1-piperidyl)ethoxy]tropane bismethiodide, m. above 305°; 3-[3-(1-piperidyl)propoxy]tropane, b0.1 115°; 3-[3-(1-piperidyl)propoxy]tropane bismethiodide, m. above 305°; 3-[2-(1-pyrrolidyl)ethoxy]tropane, b2.8 134°, nD25 1.4932; 3-[2-(1-pyrrolidyl)ethoxy]tropane bismethiodide, m. 313-4°; 3-(2-diethylaminoethoxy)pseudotropane, b0.25 109-12°, nD25 1.4775; 3-(2-diethylaminoethoxy)pseudotropane bismethiodide, m. 307-8° (decomposition); 3-(3-diethylaminopropoxy)tropane, b0.2 94-6°; 3-(3-diethylaminopropoxy)tropane bismethiodide, m. 300° (decomposition). 3-(2-Diethylaminoethylmercapto)tropane can be prepared by heating 3-bromotropane with 3-diethylaminoethylmercaptan in NaOH solution 1-Methyl-4-(3-tropanyl)-1,2,4,5-tetrahydro-1,4-benzodiazepine bismethiodide, m. 264-7° (from H<sub>2</sub>O) (decomposition). Similarly the following compds. are prepared: 3-(2-phenylmethylaminoethylamino)tropane, b0.1 167-73°; 1-methyl-4-(3-tropanyl)-1,2,4,5-tetrahydro-1,4-benzodiazepine, b0.3 170-2°; 3-(2-phenylethylaminoethylamino)tropane, b0.6 174-7°; 3-(2-phenylethylaminoethylamino)tropane 8-methiodide, m. 226-8° (decomposition); 1-ethyl-4-(3-tropanyl)-1,2,4,5-tetrahydro-1,4-benzodiazepine, b0.5 174-8°; 1-ethyl-4-(3-tropanyl)-1,2,4,5-tetrahydro-1,4-benzodiazepine bismethiodide, m. 269-71°; 1-ethyl-4-(3-tropanyl)-1,2,4,5-tetrahydro-1,4-benzodiazepine 8-

methiodide, m. 235-8°; 1-ethyl-4-(3-tropanyl)-1,2,4,5-tetrahydro-1,4-benzodiazepine bismethobromide, m. 262-2.5° (decomposition). 2,5-Diethoxytetrahydrofuran (160 g.), 150 ml. H<sub>2</sub>O, and 0.13 ml. concentrated HCl stirred at 48-50° 2 hrs., cooled to 25°, 202 g. di-Et acetonedicarboxylate followed by 100 ml. H<sub>2</sub>O and 107 g. PhCH<sub>2</sub>NH<sub>2</sub>.HCl added, the mixture stirred overnight, treated with 250 ml. HCl, and heated to 103° to remove H<sub>2</sub>O, the residue filtered off, the filtrate made basic with 250 ml. 35% NaOH, 500 g. K<sub>2</sub>CO<sub>3</sub> added, and extracted 3 times with Et<sub>2</sub>O gave 102 g. 8-benzylnortropanone, b0.4 134-7, nD<sub>25</sub> 1.5562. Similarly are prepared: 3-(2-diethylaminoethylamino)-8-benzylnortropane, b0.25 161-8°, nD<sub>25</sub> 1.5235; 3-(2-diethylaminoethylamino)-8-benzylnortropane trihydrochloride, m. 264-6° (decomposition); 3-(2-diethylaminoethylamino)-8-benzylnortropane bismethiodide, m. 255-7°; 3-(2-diethylaminoethylamino)-8-(4-methoxybenzyl)nortropane; 3-(2-diethylaminoethylamino)-8-(4-methoxybenzyl)nortropane trihydrochloride, m. 277-8° (decomposition); 3-(2-diethylaminoethylamino)-8-(4-methoxybenzyl)nortropane bismethiodide, m. 229-30°; 3-(2-diethylaminoethylamino)-8-(2,3-dimethoxybenzyl)nortropane; 3-(2-diethylaminoethylamino)-8-(2,3-dimethoxybenzyl)nortropane trihydrochloride, m. 234-7°; 3-(2-diethylaminoethylamino)-8-(2,3-dimethoxybenzyl)nortropane bismethiodide, m. 226-8°; 3-(2-diethylaminoethylamino)-8-(3,4-methylenedioxybenzyl)nortropane; 3-(2-diethylaminoethylamino)-8-(3,4-methylenedioxybenzyl)nortropane trihydrochloride, m. 275-6° (decomposition); 3-(2-diethylaminoethylamino)-8-(3,4-methylenedioxybenzyl)tropane bismethiodide, m. 234-7°; 3-(2-diethylaminoethylamino)-8-(4-chlorobenzyl)nortropane; 3-(2-diethylaminoethylamino)-8-(4-chlorobenzyl)nortropane trihydrochloride, m. 273-5°; 3-(2-diethylaminoethylamino)-8-(2-chlorobenzyl)nortropane; 3-(2-diethylaminoethylamino)-8-(2-chlorobenzyl)nortropane bismethiodide, m. 232-4°; 3-(2-diethylaminoethylamino)-8-(2-methoxybenzyl)nortropane trihydrochloride, m. 248-51°; 3-(2-diethylaminoethylamino)-8-(2-methoxybenzyl)nortropane bismethiodide, m. 218.5-21.5°; 3-(2-diethylaminoethylamino)-8-phenylnortropane; 3-(2-diethylaminoethyl)methylamino-8-phenylnortropane. Hydrated pseudopelletierine (29.8 g.), 26 g. 2-(1-piperidyl)ethylamine, 600 mg. ZnCl<sub>2</sub>, and 150 ml. C<sub>6</sub>H<sub>5</sub>CH<sub>3</sub> refluxed 64 hrs. using a separator to collect the H<sub>2</sub>O formed, the product cooled, washed with 50 ml. saturated K<sub>2</sub>CO<sub>3</sub> solution, and the aqueous layer extracted with 4 50-ml. portions of C<sub>6</sub>H<sub>6</sub> yielded 27.8 g. 3-[2-(1-piperidyl)ethylimino]-9-methylgranatanine (II), b1 164-76°, nD<sub>25</sub> 1.5235. To 27.8 g. II in 40 g. 4-methyl-2-pentanol is added slowly 9.2 g. Na in 200 ml. PhMe, the mixture refluxed 0.5 hr., 30 ml. H<sub>2</sub>O added, cooled, the aqueous layer saturated with K<sub>2</sub>CO<sub>3</sub>, extracted with 3 100-ml. portions of PhMe, the PhMe layers concentrated, dissolved in 50 ml. MeOH, 15 g. phenyl isothiocyanate stirred in, and the precipitate (34.4 g.) filtered off and recrystd. from AcOEt. By fractional precipitation from MeOH 2 isomers of 1-[2-(1-piperidyl)ethyl]-1-3-(9-methyl)granatanyl-3-phenylthiourea, isomer A, m. 174.5-6° (prisms from AcOEt), and isomer B, 173-4.5° (needles) are obtained. Also prepared were: 3-[2-(1-piperidyl)ethylamino]-9-methylgranatanine trihydrochloride (from isomer A), m. 285-7° (decomposition); 3-[2-(1-piperidyl)ethylamino]-9-methylgranatanine trihydrochloride (from isomer B), m. 276° (decomposition); 1-(2-diethylaminoethyl)-1-(3-tropanyl)-3-phenylthiourea, m. 170.5-2°; 3-(2-diethylaminoethylimino)tropane, b0.6 117-31°; 3-(2-diethylaminoethylamino)tropane; 1-(2-diethylaminoethyl)-1-(3-pseudotropanyl)-3-phenylthiourea, m. 138-9.5°; 3-(2-diethylaminoethylamino)pseudotropane trihydrochloride, m. 276° (decomposition); 3-(2-diethylaminoethylamino)pseudotropane bismethiodide, m. 279-81° (MeOH); 3-[2-(1-pyrrolidyl)ethylamino]-9-methylgranatanine, b2 155-7°, nD<sub>25</sub> 1.5102; 1-[2-(1-pyrrolidyl)ethyl]-1-[3-(9-methyl)granatanyl]-3-phenylthiourea, m. 173-4°; 3-[2-(1-pyrrolidyl)ethylamino]-9-methylgranatanine bismethiodide, m. 278° (decomposition); 3-(2-diethylaminoethylamino)-9-methylgranatanine, b0.6 128-30°, nD<sub>25</sub> 1.4920; 1-(2-diethylaminoethyl)-1-(9-

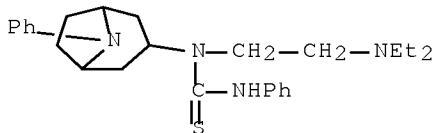
methylgranatanyl)-3-phenylthiourea, isomer B, m. 188-90°; 1-(2-diethylaminoethyl)-1-(9-methylgranatanyl)-3-phenylthiourea, isomer A, m. 135-6°; 3-(2-diethylaminoethylamino)-9-methylgranatanine trihydrochloride, isomer A, m. 278° (decomposition) [trihydrochloride of isomer B, m. 185°; bismethiodide of isomer A, m. 277-9° (decomposition)]; 1-(2-diethylaminoethyl)-1-{3-[8-(2-chlorobenzyl)nortropanyl]}-3-phenylthiourea, m. 124-6°; 1-(2-diethylaminoethyl)-1-[3-(8-phenyl)nortropanyl]-3-phenylthiourea, m. 161-3°. 3-(2-Diethylaminoethylamino)tropane (4.0 g.) treated with 1.7 ml. allyl isothiocyanate yielded 3.6 g. 1-(2-diethylaminoethyl)-1-(3-tropanyl)-3-allylthiourea, m. 97-100°. Similarly the following compds. are prepared: 1-(2-diethylaminoethyl)-1-(3-tropanyl)-3-ethylthiourea, m. 122-4°; 1-(2-diethylaminoethyl)-1-(3-tropanyl)-3-(4-ethoxyphenyl)thiourea, m. 160-1°; 1-(2-diethylaminoethyl)-1-[3-(8-benzyl)nortropanyl]-3-phenylthiourea, m. 138-9°; 1-(2-diethylaminoethyl)-1-{3[8-(3,4-methylenedioxybenzyl)]nortropanyl}-3-phenylthiourea, m. 148-9°; 3-[(2-diethylaminoethyl)acetylamino]tropane, b0.09 142-4°, nD25 1.4980 (picrate, m. 190-200°) (from EtOH); 3-[(2-diethylaminoethyl)ethylamino]tropane, b2 142°, nD25 1.4845 (bismethiodide, m. 230-1°) (decomposition); 3-[(2-diethylaminoethyl)ethylamino]tropane bismethiodide, m. 226° (decomposition); 3-[(2-diethylaminoethyl)propionylamino]tropane, b0.5 160°, nD28 1.4940-5 (picrate, m. 173-6°) (from aqueous HCONMe<sub>2</sub>); 3-[(2-diethylaminoethyl)propylamino]tropane, b0.1 119-26°, nD28 1.4835 [picrate, m. 223° (decomposition); bismethiodide, m. 203-9° (decomposition)]; 3-[(2-diethylaminoethyl)butyrylamino]tropane, b0.7 162-6°, nD25 1.4935 (picrate, m. 194-6°); 3-[(2-diethylaminoethyl)butylamino]tropane, b0.1 125-30°, nD25 1.4839 [picrate, m. 208-10° (decomposition)]; 3-[(2-diethylaminoethyl)acetylamino]-8-phenylnortropane, b0.2 183-98°, nD28 1.5470; 3-[(2-diethylaminoethyl)ethylamino]-8-phenylnortropane, b0.9 180-4°, nD30 1.5370; 3-[(2-phenylethylaminoethyl)formylamino]tropane, b0.1-0.2 200-7°; 3-[(2-phenylethylaminoethyl)formylamino]tropane, b0.9 166-72°, nD25 1.5131 (picrate, m. 192-4°); 3-[(2-phenylethylaminoethyl)methylamino]tropane, b1.6 182-7°, nD24 1.5518.

IT 123935-68-2

(Derived from data in the 6th Collective Formula Index (1957-1961))

RN 123935-68-2 CAPLUS

CN Urea, 1-(2-diethylaminoethyl)-3-phenyl-1-(8-phenyl-3-nortropanyl)-2-thio- (6CI) (CA INDEX NAME)

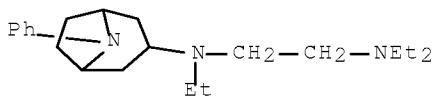


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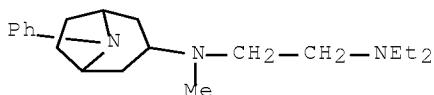
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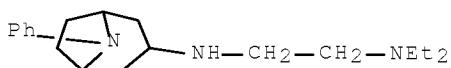
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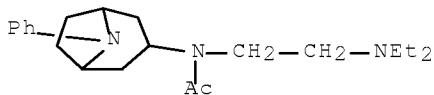
RN 102463-23-0 CAPLUS  
 CN Nortropane, 3-[(2-diethylaminoethyl)methylamino]-8-phenyl- (6CI) (CA INDEX NAME)



RN 102709-02-4 CAPLUS  
 CN Nortropane, 3-[(2-diethylaminoethyl)amino]-8-phenyl- (6CI) (CA INDEX NAME)



RN 110147-72-3 CAPLUS  
 CN Nortropane, 3-[N-(2-diethylaminoethyl)acetamido]-8-phenyl- (6CI) (CA INDEX NAME)



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 ACCESSION NUMBER: 1957:86037 CAPLUS  
 DOCUMENT NUMBER: 51:86037  
 ORIGINAL REFERENCE NO.: 51:15606g-i,15607a-c  
 TITLE: Heterocyclic alcohol diammonio esters  
 PATENT ASSIGNEE(S): Cutter Laboratories, Inc.  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Unavailable  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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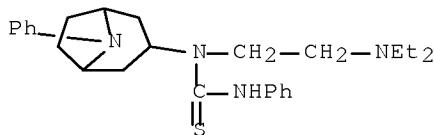
AB Esters containing two quaternary nitrogens, a trialkyl N being on the acid moiety and a heterocyclic N on the alcohol moiety are useful as hypotensor agents. Thus, to make 2-(1-ethylpiperidinium)ethyl 3-(trimethylammonium)propionate diiodide (I), 10.0 g. 1-ethyl-1-(2-hydroxyethyl)piperidinium iodide (II) was first acylated 1 hr. with 26 g. I(CH<sub>2</sub>)<sub>2</sub>COCl (III) on a steam bath. This product was washed with Et<sub>2</sub>O, MeOH and then Et<sub>2</sub>O to yield a residue which was dissolved in an MeOH-dioxane (10 ml.:25 ml.) and mixed with 2.1 g. Me<sub>3</sub>N in 16 ml. dioxane. After 3 days, 10.6 g. I, m. 169-71° (from MeOH), separated. Directions are given for similar reactions to yield the following 2-(substituted-ethyl)-3-(trimethylammonium)propionate diiodides (substituent on C-2 of ethyl, yield and m.p., crystallization solvent given): 1-methylpiperidinium, 52%, 170-1°, MeOH-Et<sub>2</sub>O (IV); 1-methylpyrrolidinium, 81%, 190°, IV; 4-methylmorpholinium, 61%, 188-90°, MeOH. An alternative procedure was represented by refluxing 10 g. 2-(4-methyl-1-piperidyl)-2-propyl 3-(dimethylamino)propionate (V), in 500 ml. Me<sub>2</sub>CO 1 hr. with 20 g. MeI. Upon cooling, the mixture yielded 16.3 g. 2-(1,4-dimethylpiperidinium)-2-propyl 3-(trimethylammonium)propionate diiodide (VA), m. 170-2° (from wet Me<sub>2</sub>CO). II was prepared in 60% yield by refluxing 24 hrs. 13.5 g. 2-iodoethanol in 50 ml. MeOH with 9.0 g. 1-ethylpiperidine. The oily II which separated on cooling slowly solidified. Crystallization of this solid from Me<sub>2</sub>CO-MeOH (100 ml.:50 ml.) yielded 10.3 g. II, m. 240°. 1-(2-hydroxyethyl)-1-methylpiperidinium iodide, m. 235-8°, was similarly prepared in 93% yield. Equimolar quantities of 4-methylpiperidine and propylene oxide, when refluxed 4.5 hrs. and distilled, yielded 80% 1-(4-methyl-1-piperidyl)-2-propanol (VI), b. 210-12°. VI was slowly added to 1 mole acryloyl chloride in C<sub>6</sub>H<sub>6</sub> and this mixture then refluxed 2.5 hrs. The C<sub>6</sub>H<sub>6</sub> solution, after washing with cold saturated NaCl solution and excess Na<sub>2</sub>CO<sub>3</sub> solution, yielded 69% 2-(4-methyl-1-piperidyl)-2-propyl acrylate (VII), b<sub>2.5</sub> 85°. When 1 mole gaseous Me<sub>2</sub>NH was passed into cold VII and this mixture held 17 days at room temperature (sealed tube), distillation (93-8° at 1.5 mm.) yielded V containing about 20% VII, satisfactory for producing VA. III (b<sub>18</sub> 75-80°) was prepared in 75% yield by refluxing I(CH<sub>2</sub>)<sub>2</sub>CO<sub>2</sub>H (36 g.) with 14 ml. PCl<sub>3</sub> 5 hrs. and distilling Using an ion exchange column (Cl form), I was converted to its dichloride, m. 200-1°. The dinitrate, m. 142°, and the dibitartrate, m. 123-6°, of I were prepared from I and the appropriate Ag salt. Picric acid and I yielded I dipicrate, m. 182-3°. In most examples, analyses are given.

IT 123935-68-2

(Derived from data in the 6th Collective Formula Index (1957-1961))

RN 123935-68-2 CAPLUS

CN Urea, 1-(2-diethylaminoethyl)-3-phenyl-1-(8-phenyl-3-nortropanyl)-2-thio-(6CI) (CA INDEX NAME)



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